ARMED FORCES EPIDEMIOLOGY BOARD

6-7 December 2005

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Day One

Pope Club
5504 Reilly Street
Pope Air Force Base
Fort Bragg, North Carolina 28307-5127

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PROCEEDINGS

DR. POLAND: Welcome all to the meeting of the Armed Forces Epidemiological Board. We have a number of important topics on our agenda today, so why don't we get started. Ms. Embrey, would you call the meeting to order?

MS. EMBREY: Absolutely. Thank you, Dr. Poland. As the Designated Federal Official for the Armed Forces Epidemiological Board, a Federal Advisory Committee to the Secretary of Defense, which serves as a continuing scientific advisory body to the Assistant Secretary of Defense for Health Affairs and the Surgeons General of the Military Department, I hereby call this meeting to order. COL Maul, wherever you are, please accept my appreciation for your willingness to host this meeting on our behalf, and the outstanding support that you and your staff have given us to enable us to have this meeting here today.

DR. POLAND: Thank you, Ms. Embrey. Before we go around the table and introduce ourselves, I do want to recognize our new members and one returning for whom this is their first meeting. The first is a friend and colleague at Kaplan who presented to the Board at San Diego a year ago, and joins us from the Division of Epidemiology at the University of Minnesota School of

Public Health in Minniapolis.

His honors and awards are numerous, but a small selection include an International Service Citation from the American Heart Association, several honorary memberships in foreign medical societies, many occasions as a guest lecturer, and the National Award of Merit from the American Heart Association.

Ed, welcome.

(Applause.)

DR. POLAND: We also have with us Dr. Kevin McNeill who comes to us from Mississippi, where he serves as the state epidemiologist, as director of the Mississippi Public Health Laboratory and the principal investigator of the CDC bioterrorism Preparedness Cooperative.

Dr. McNeill received the U.S. Army Legion of Merit Award and the WRAIR Director's Award in 1999, and also served as Chief of Preventative Medicine Service at Eisenhower Army Medical Center, and again at Fort Sam Houston and then at Fort Jackson and here at Fort Bragg.

Dr. McNeill, welcome.

(Applause.)

DR. POLAND: Our third new member with us today is Dr. Joseph Silva, Jr. Dr. Silva currently serves as Dean Emeritus at the U.C. Davis School of Medicine. He

has previously served as professor and chairman of internal medicine at U.C. Davis, as professor of medicine at the University of Michigan Medical School and as a lecturer at the University of Texas, San Antonio.

In addition to his academic appointments he served as a consultant for Kaiser-Permanente Hospital for the VA hospitals in Ann Arbor and northern California, and as staff physician at the U.S. Air Force Medical Center at Lackland. He's received numerous awards and honors from medical societies and hospital associations.

Joe, welcome.

DR. SILVA: Thank you.

(Applause.)

DR. POLAND: Last, but certainly not least, we have our returning member, Dr. Adil Shamoo. Some of you may remember Dr. Shamoo from approximately a year ago when he served as a consultant on the Board. We are very pleased that he has been able to rejoin us. He is currently serving as editor-in-chief and accountability and research at the University of Maryland School of Medicine. Recent assignments include consultant, Friends Research Institute in Baltimore, Maryland; a member of National Human Research Protection Advisement Committee; Professor and former chairman Department of Biochemistry and molecular biology.

That one makes my palms sweat.

(Laughter)

DR. POLAND: University of Maryland, School of Medicine. And member of the center for biomedical ethics, University of Maryland. Dr. Shamoo comes to the U.S. from Bagdad, Iraq in the 1960s and has established himself as a expert in medical ethics.

Welcome back.

(Applause.)

DR. POLAND: Now if we could go around the room and introduce ourselves. We certainly have an impressive gathering of military, academic, and civilian medical minds here today. Ms. Embrey, we'll get started with you.

MS. EMBREY: I'm Ellen Embrey, I'm with the Department of Defense and I'm glad to be here.

DR. PARKINSON: Good morning, Mike Parkinson with Lumenos.

DR. BLAZER: Dan Blazer, good morning, from Duke, just up the road.

MR. SHAMOO: Adil Shamoo.

MR. BAKER: Sue Baker from Johns Hopkins School of Public Health.

DR. LEDNAR: Wade Lednar, Eastman Kodak.

DR. BROWN: I am Mark Brown. I'm from the

Department of Veteran's Affairs.

CPT NAITO: Neil Naito from Uniform Surgeons University.

COL UNDERWOOD: Paula Underwood, Army Surgeon Generals Office.

CDR CARPENTER: David Carpenter, Canadian Forces Medical Liaison Officer.

DR. GRAY: Greg Gray, University of Iowa, College of Public Health.

DR. HALPERIN: Bill Halperin, New Jersey Medical School, Department of Health.

DR. McNEILL: Kevin McNeill from the Mississippi Department of Health.

DR. LEMASTERS: Grace Lemasters, College of Medicine, University of Cincinnati.

DR. CATTANI: Jackie Cattani, School of Public Health from the University of South Florida, Tampa.

DR. OXMAN: Mike Oxman, University of California, San Diego, and the VA Medical Center in San Diego.

DR. SILVA: Joe Silva.

DR. LAUDER: Tamara Lauder, Medicine Rehab, St. Germain, Wisconsin.

DR. KAPLAN: Ed Kaplan, University of

Minnsota.

COL GIBSON: Roger Gibson, Executive Secretary, Armed Force Epi Board.

DR. POLAND: Greg Poland, Mayo Clinic College of Medicine, Rochester, Minnesota.

CPT JOHNSTON: Richard Johnston, British Liaison Officer.

MAJ KILIAN: Dennis Kilian, Joint Staff.

CDR MCMILLAN: David McMillan, Headquarters, Marine Corps.

LTC SNEDECOR: Mike Snedecor, Air Force Surgeon Generals Office.

CPT KILBANE: I'm Ed Kilbane. I'm from the Bureau of Medicine and Surgery from the U.S. Navy.

LCDR SCHWARTZ: I'm LCDR Erica Schwartz, I'm the Coast Guard Preventative Medicine Liaison.

LTC HACHEY: Wayne Hachey, DoD Public Affairs.

(The audience members introduced themselves.)

DR. POLAND: I also want to thank, COL Maul and his staff at Fort Bragg and Pope Air Force Base for hosting this meeting of the Armed Forces Epidemiology Board.

Our distinguished guest here with us this morning is Dr. Mullick from AFIP. She will be later.

Thank you all for attending. COL Gibson has some administrative remarks before we begin the morning session.

COL GIBSON: I also want to thank COL Maul for hosting this meeting. He's done a wonderful job of putting together an excellent tour of Fort Bragg. He's going to have some wonderful words about Fort Bragg in just a few minutes.

I particularly want to thank LTC Ponce. Renee helped us put this meeting together. She was our point person down here at Bragg for the meeting, and did a wonderful job. Very, very helpful.

Also thanks for Marcy Newberry here at the Pope Club for coordinating the conference space and the support from the club.

We get four continuing education credits for the meeting here today. To receive the credits you need to sign the physician's attendance roster today, since this is the day we are going to get the credits, and complete the evaluation form for the meeting, and hand it in tomorrow.

I want to inform everyone that this is a transcribed meeting. Before speaking, please state your name so the transcriber can keep track of who has said what. And then the meeting transcripts will be available

on the AFEB website in a few weeks, as soon as we get it back from the transcriber. And the slides will be posted also on the AFEB website. We have a limited number of hard copies of the slides back here, but all of the slides, as soon as the briefers bless them, they will go up on the AFEB website. Please sign the attendance roster as well, if you haven't done that already.

Tonight we are eating dinner as a -- the Board is eating dinner at the Huske Hardware House and Brew Club, in historic downtown Fayetteville. A wonderful place. So it's open to all attendees, and if we could get a quick show of hands on how many are going to come to dinner with us tonight, I would really appreciate it.

(Show of hands.)

COL GIBSON: For this meeting we'll have refreshments available both morning and the afternoon. We have a catered working lunch for all the attendees. It's $6.95. It will be right here at the Pope Club. If you don't want to eat with us, there are other places on base, both on Fort Bragg and on Pope where you can get pizza and other types of food.

The tour tomorrow, the tour is going to run just a little longer than we originally planned. We thought we would back here by 3:00. It will probably be

a little closer to 4:00. Those of you who have to leave early, we will have cars following that can bring us back here. We are going to a jump site and watch parachuting, and according to Renee, we have some other events, such as hand grenades and a few other things that we will be able to see. If you could, give me a quick show of hands on how many plan on going on the tour with us tomorrow.

(Show of hands.)

COL GIBSON: Severine wanted me to remind you, if you want to get your coats out of this area, they have got a coat closet back here. She'll come around and pick them up. Just raise your hand or take your coat to her. She'll be happy to take care of it.

Finally, the next AFEB meeting will be July 21st and 22nd -- excuse me, February 21st, 22nd. That's the third Tuesday and Wednesday of February. Portsmouth Naval Hospital in Norfolk will be hosting the meeting. The tentative agenda includes population health and emerging infectious issues, and some discussion of traumatic brain injury. For more information, check the AFEB website.

DR. POLAND: Before we get to the introduction of speakers, what I would like to do and the Board hasn't done for a while, is have everybody stand for one minute of solemn silence to recognize our fellow citizens who

have fallen in service to their county. I would like us to stand for a minute silently to reflect on that, and also to sort of quiet our minds as we get ready to do the important work that is before us.

(All stand for a moment of silence.)

DR. POLAND: Thank you all very much. A small way in which you can remember certainly the last full measure of sacrifice that has been made on our and many other people's behalf.

Okay, our first speaker, COL Maul, wanted to take a few minutes to welcome the Board to Fort Bragg. Thank you, Col Maul.

COL MAUL: Good morning. I generally don't like podiums, that is why I am moving around. Come on, the Huske Hardware Store is a nice restaurant. Just because it used to be a hardware store, you'll have a good time there. And please take note of renovations that are ongoing in downtown Fayetteville. It really is a historic place and various groups are doing a lot of great things to update it and so forth.

On behalf of MG Packet, the Acting Corp Commander of XVIII Airborne Corps and Fort Bragg, and the highly esteemed soldiers and civilian employees of Womack Army Medical Center, I would like to welcome you all. Ms. Embrey, members of the Board, other attendees, welcome

you all to our corner of North Carolina.

I am the commanding officer of Womack Army Medical Center; have been there now for about 17 months. Came here from being the Command Surgeon at U.S. Central Command, where I got to know Ms. Embrey extremely well. We worked very closely on working some tough force protection issues for our soldiers, sailors, airmen, marines, coast guard deployed in the CENCOM AOR.

I am especially pleased that the rain stopped from yesterday, so that you all have an opportunity to witness firsthand the trademark Carolina blue sky here. We're very proud of that.

Before I go any further though, I would like to show you a little video that we had made locally, as a matter of fact, that we just took ownership of about a little over a month ago. It's a marketing video for Womack and pun intended, it's bragging about Womack. So if we could run the video and I will close up with a few comments afterward.

Can we back it up to the beginning. We're way into the meat of this. Murphy is always with us.

(Video played.)

COL MAUL: That gives a little snapshot about things we do. But in addition to our three main activities of providing high quality health care to our

beneficiaries, supporting the global war on terrorism, and executing premiere training programs, we are also looking ahead. And I am not talking about specifically at BRAC, although that is pretty much the buzz word at DoD these days. Even before BRAC, we are getting into the reorganization of the 82d Airborne Division now in concert with the Army's Campaign Plan. We are also going through transformation of the Special Operations Forces and so forth. And also some relocation of forces and units from Europe to Fort Bragg.

So put all of that together in the next five physical years, the Army's largest troop population is going to get even larger. We are anticipating about another, in round figures, I know these numbers are subject to change, about ten to 11,000, 12,000 active duty forces coming in, and about 25,000 total beneficiaries with their family members, so forth. So bottom line there I think, is as long as there's a U.S. Army, there will be a Fort Bragg. And as long as there's a Fort Bragg, there will be a Womack Army Medical Center. So we are making plans now to support that increase in population.

I will tell you, though, that even before modulary transformation, BRAC, and all of these sorts of things, Fort Bragg has continued to grow. On your tour

you will notice several construction projects on the installation. That was preprogrammed to the tune of about 200 million dollars a year for the next five years, a billion dollars total, to either put into new construction or renovate old buildings on the post, and so forth. So in addition to a tremendously high opstempo supporting the Global War on Terrorism and everything that goes with that, it is a busy place anyway. You will get a glimpse of that too when you visit some of the training sites and that type of thing. So the point is, never a dull minute at Fort Bragg. We are happy to be here, and we are happy to have you here, and we just wish you the best in the next few days, and hope you enjoy your stay on Fort Bragg. Don't be shy. If there is anything you need to know, want to know, would like to know, I have empowered Renee back there, COL Ponce to answer any and all questions.

(Laughter.)

COL MAUL: She will have an answer. It may not be the right one, but in all seriousness, please enjoy yourselves here. We do welcome you to Fort Bragg. Come back and see us when you can spend more time here. We've got lots to show you if you're interested, especially at Womack. I don't believe that is on your tour agenda, but please come back any time. We will walk you through that too. I'll be glad to show it off.

Now, before I give up the microphone, any questions that I could answer for you right now?

(No response.)

COL MAUL: Okay. Hearing none, ma'am, thank you for bringing the Board to Fort Bragg, and enjoy your stay. Thanks a lot.

(Applause.)

DR. POLAND: Thank you COL Maul. On behalf of the entire Board and the Office of the Assistant Secretary of Defense for Health Affairs, we would like to present a Plaque and Certificate of Appreciation. We would also like to present LTC Ponce with a Certificate of Appreciation and an AFEB coin for her outstanding work in helping to coordinate this meeting.

So presented to COL Ronald A. Maul and staff at the Womack Army Medical Center at Fort Bragg, North Carolina, in appreciation for your key support during the December 2005 meeting of the AFEB. Thank you.

COL MAUL: Thank you so much. I appreciate it.

(Applause.)

DR. POLAND: The Office of the Secretary of Defense presents this Certificate of Appreciation to LTC Renee Ponce for superb leadership, excellent organizational skills and outstanding professional

knowledge and willingness to assist and cooperate in all issues supporting the Armed Forces Epidemiological Board, December 2005 meeting. So LTC Ponce, thank you.

LTC PONCE: My pleasure, thanks a lot.

(Applause.)

DR. POLAND: This morning we will hear a series of presentations related to the occupational health and environmental implications of chemical munitions. There is a question before the Board requiring an official recommendation. That question is under Tab 2.

To start us off we have COL Peter Cooper, Acting Director of Operations, U.S. Army Chemical Materials Agency, at the Aberdeen Proving Grounds. COL Cooper will present the question to the Board.

Welcome, COL Cooper.

COL COOPER: Thank you. I tried to do my homework and do my G2 and figure out what you all did and what the Board was. I didn't even know there was an AFEB until about two months ago. I would like to thank you up front for your service to our nation. I think that what you are doing here is important as evidenced by how we opened the session in remembering our fallen comrades. So again, thank you very much.

I'm here to open the first topic and actually

request the Board's support. And so in order to do that, I need to tell you a little bit about who we are and what we do. As I look at the make up of the Board, I realize that you may not understand what the Chemical Materials Agency is. Again, I'm COL Pete Cooper. I am the Acting Director of Operations of the Chemical Materials Agency. The Chemical Materials Agency has been charged by our country and has the national imperative to safely and securely store the nation's stockpiled chemical weapons.

Just to give you an order of magnitude of what we're talking about, the original stockpile of the nation's chemical munitions was in the order of 30,000 agent tons. That is just the weight of the agent, not the weight of the munitions. At one of our sites, Desert Chemical Depot, we have destroyed over one million individual items of munitions already. And in the inventory and still remaining in the inventory is over 1.8 million individual items of chemical munitions. So we are talking about a very large stockpile that is managed by tens of hundreds of both Department of Defense civilians. We only have about 20 total soldiers, and tens of hundreds of contractors under the employment of the Chemical Materials Agency. So that is the Chemical Material Agency and the magnitude of what we're talking about. You will hear more about this as we get into the

topic later.

What brings me here today is actually an article in the American Journal of Public Health titled "Mortality in U.S. Army Gulf War Veterans exposed to 1991 Khamisiyah Chemical Munitions Destruction," by Tim Bullman, et al, August 2005.

In March 1991 two large Iraqi weapons stored at Khamisiyah -- excuse me -- two large Iraqi weapon storage sites in Khamisiyah, Iraq, were destroyed by the United States Army. It was later discovered that there were chemical warfare agents (Sarin and cyclosarin) present in both intact and damaged rockets. The article postulates an association between extremely low level short-term exposures to the down-wind plume following chemical munitions destruction at Khamisiyah and increased risk of brain cancer.

If this is true, the association could have profound effects on U.S. Army Chemical Material Agency mission to safely destroy -- safely store and destroy these chemical munitions. The potential for increased risk to workers, the public, could require changes to demilitarization design, personal protection equipment, medical surveillance, environmental monitoring and chemical and accident, or instance response. All of our sites are surrounded by local communities, so we are not

only talking about the safety of our local community -- of our workers, but also to our surrounding local community.

In light of these concerns raised by this article, the chemical Materials Agency would like the Board to consider taking three questions on for us, and helping us understand the science and the biology behind what the article speculates.

Our three questions are, we would like you to comment on the conclusions presented by the authors, particularly with respect to biological plausibility of an association between the low-dose short-term chemical munitions exposure and brain cancer.

Does the evidence presented by Bullman constitute sufficient evidence to warrant modifications in current occupational health processes and environmental safety measures for chemical agents?

If more research is needed in this area, how should the research plan be structured in order to most efficiently test the hypothesis while minimizing the risk to workers and the public, time spent and resources expended? Which organization is best suited to lead this effort?

Let me just leave one final comment with the Board. Just as our soldiers, I don't mean to make a

direct comparison to the soldiers, but as our soldiers are fighting the war on terrorism, we have a very dedicated population of civilian and contract employees who are every day entering igloos, moving munitions around, and working the national imperative to rid our nation of these weapons that our country has decided that we would no longer use.

With that, ladies and gentlemen of the Board, any questions?

DR. POLAND: Thank you, COL Cooper. Our next speaker is Dr. Timothy Bullman, lead author of the American Journal of Preventative Health article -- public health article on mortality in the U.S. Gulf War Veterans. That is part of, right under the question under Tab 2.

DR. BLAZER: Very quickly, I was actually on the advisory committee that oversaw the study of this ___ to the medicine which this article came. For that reason, I will have to recluse -- I will sit through this, but I will recluse myself from any part in this discussion.

DR. POLAND: Okay, thank you. Dr. Bullman, we're delighted to have you attend this meeting to discuss your paper.

DR. BULLMAN: Good morning. My presentation

this morning, we'll review the Mortality study of Army Gulf War Veterans, potentially exposed to nerve agents during Gulf War I. Between March 10, and March 13, 1991, U.S. units stationed in Iraq, blew up Iraqi munitions stored at Khamisiyah Iraq. Subsequent inspections by U.N. Commission of the site revealed the presence of debris characteristic of chemical munitions and also intact munitions containing both Sarin and cyclosarin. This raised concern that the troops present at Khamisiyah during the destruction of the munitions might have been exposed to Sarin or other chemical or biological warfare agents.

Next slide please. The genesis of this study dates to the spring of 1999 when the Army Surgeon Generals Office contracted with IOM conduct several studies assessing the morbidity associated with exposure at Khamisiyah. Our office was asked to be a co-investigator because of the Persian Gulf National Survey Health Data we've collected.

After initial meetings with IOM it was decided that because our office also had access to various data bases that could be used to determine vital status of veterans, that a mortality study of veterans potentially exposed to nerve agents at Khamisiyah should also be conducted.

This study would assess overall and cause specific mortality risks associated with the Khamisiyah model exposure.

Next slide please. Oh, in the spring of 2000 we received the following: 351,121 Army Gulf War Veterans, for whom exposure status had been determined using the so-called 2000 plume model. We use this file along with data from other resources to conduct our analysis.

Third slide please.

The first model to assess the potential of exposure at Khamisiyah was developed in 1997 and is referred to as the 1997 plume model. This model developed jointly by DoD and the CIA used dispersion and meteorologic models, data reconstructed from demolitions, troop locations at the time level to generate a potential hazard area covering the four days during which U.S. troops detonated Iraqi weapons stored at Khamisiyah. In 2002 DoD refined the '97 model by adding disposition and degradation data, and revising the meteorologic model and using company level location, rater than the larger battalion level data.

Slide four. I'm sorry, go back.

Using the file provided by DoD, we identified 100,487 exposed, 224,980 unexposed, 25,574 exposure

status, unknown. The inability to determine exposure was because of missing or incomplete unit information, or service dates for a veteran.

Vital status for all veterans was determined using a VA data base known as BURLES and a file of deaths reported to the Social Security Administration. Cause of death data was obtained by the National Death Index. The National Death Index is a file of deaths reported to the National Center for Health Statistics by various state vital statistics offices. At the time this analysis was conducted, cause of death was available only through 2000. Therefore, this study's vital status follow-up extended from the date the veteran left the Gulf theater alive to the earlier of either the date of death or December 2000.

Next slide please. Using the BURLES and SSA file of deaths, we identified 1,179 deaths among exposed, 2,696 deaths among unexposed, and 341 deaths among exposure status unknown. Cause of death data was retained for 96 percent of exposed deaths, 95 percent of unexposed deaths, and 92 percent of exposure status unknown.

Next slide please. Demographic and military service characteristics were obtained from Defense Manpower Data Center. Number of days exposed as well as

exposure status was provided by the DoD Deployment Health Support Directorate.

During the course of this analysis it was decided to add all well fire smoke exposure data to the model. This data was obtained from the Army group known as CHPPM or U.S. Army Center for Health Promotion and Preventative Medicine.

Next slide please. The statistical analysis used in this study assessed cause specific mortality risk associated with exposure by comparing exposed to unexposed. Specific analysis concluded crude death rates calculated as number of years, number of deaths per ten thousand person years at risk. Unadjusted relative risk estimates based on the crude rates, and finally adjusted relative risk estimates obtained from the cause proportional hazard model.

Next slide please. Covariats included in the cause proportional hazard model were age at entry to follow-up, race, gender, rank and unit component. Additional analysis included smoke exposure data as a covariate.

Next slide please. This table shows a distribution of exposed, unexposed and exposure status unknown amount various demographic and military service characteristics. The only noticeable difference on this

table is that you have a much higher percentage of exposure status unknown serving in a reserve unit, compared to either exposed or unexposed.

Next slide please. Here you see the frequency distribution of number days exposed. As you can see, most veterans were only exposed one day, followed by 12 percent exposed two days and 1.7 percent exposed three days. There is only one tenth of a percent exposed for all four days according to the model of exposure.

Next slide please. This table presents the analysis comparing the cause specific mortality rates of exposed to that of unexposed veterans, both with and without adjustment for covariates. Third from the left column is the crude rates, then you have the adjusted rate ratios, which is based on the Cox model which include covariant model. Then you have the 95 percent confidence intervals. As you can see for most causes, mortality rates are similar for both groups. That is the mortality rate approaches one. The one exception is for deaths due to brain cancer, where there were 25 brain cancer deaths among exposed and 27 among unexposed, resulting in almost two-fold increased risk of brain cancer associated with exposure. This isn't all the causes we looked at. This is just selected causes we

decided to put in this table. We looked at a lot of different causes.

Next slide please.

While this study did not have any dosage data, it did have a number of days exposed, or a number of days in the hazard area. Length of exposure ranged from zero, not exposed, to four days of exposure. This table compares the cause specific mortality rates of exposed veterans when stratified by number of days exposed to that of all unexposed. In other words, those exposed one day, their mortality rate is compared to all unexposed and then those were exposed two or more days. Then the mortality rates are compared to all unexposed. Your reference group here is all unexposed.

Because of the small number of veterans exposed three or four days, number of days exposed must itemized into exposed one day and exposed two or more days.

As shown in this table as length of exposure increased, so did risk of brain cancer deaths among exposed. The risk of brain cancer deaths among those exposed one day compared to all unexposed, was 1.72. Look at the very bottom there in red. Increasing to 3.26 and these are adjusted relative risk estimates -- increasing to 3.26 for those exposed two or more days.

The next slide please.

To further illustrate the association between risk of brain cancer and length of exposure, we calculate death rates per one hundred thousand persons by number of days exposed. As you can see, the rate of brain cancer per one hundred thousand persons increased steadily as the number of days exposed. For those exposed zero days, it was 11.97. For those exposed two [sic, one] days, it increased to 22.05, those exposed two days, increased to 39.83, and three days, increased to 60. So there's a pattern of increasing as length of exposure increases.

The next slide please.

To address the concern that the brain cancers identified in this study might not have been primary tumors, but may have originated in a site other than the brain, medical records were requested for all brain cancer deaths so they could be reviewed to determine which deaths were due to primary brain tumors.

Of the original 55 brain cancer deaths, 47 were determined to be primary tumors. These included -- The 47 that were determined to be primary, included 21 exposed, 23 unexposed and three exposure status unknown. Then we present the cell types that were determined for those, for whom we obtained the medical records.

Next slide please.

Limiting our analysis to only those confirmed primary brain tumors, there was still an almost two-fold statistically significant increased risk of brain cancer deaths among exposed veterans. When stratified by number of days exposed, those with confirmed primary tumors, had a 1.88 increased risk of brain cancer death. While those exposed two or more days, had a three-fold statistically significant increased risk for brain cancer death. In other words, we just limited all our previous analysis to the confirmed primary tumors, we came up with the same findings, basically that there's an increased risk for brain cancer associated with this modeled exposure.

Next slide please.

We also did a latency analysis, dividing the follow-up period into three three-year periods. Follow-up period one spanned the date the veteran left the Gulf theater alive to January 31, 1994. The second follow-up period ran from February 1, 1994 to July 31, 1997. And follow-up three extended from August 1, 1997 to December 31, 2000. Cause specific mortality risk was assessed separately for each follow-up period. As you can see, generally, the risk of brain cancer deaths increased as the length of follow-up increased. For instance, after three years of follow-up, the risk of brain cancer was 1.80; six years it approached 1, and

after nine years of follow-up, the risk increase to 3. So generally we have a pattern of risk increasing as the length of follow-up or latency increased.

Next slide please.

Addressing the potential impact that exposure misclassification could have had on our findings, we found that the exposure status of at least three exposed brain cancer deaths would have to be changed to unexposed in order the eliminate the increased risk of the brain cancer deaths. Regarding those with unknown exposure status, assigning all brain cancer death, I believe there was three of them, with exposure status unknown to either exposed or the unexposed group, did not alter our findings of increased risk of brain cancer deaths among exposed.

Next slide please.

There is also concern that the plume model might be assessing exposures other than Sarin. The only other exposure data available was smoke exposure data. To address this concern, we reassessed the risk of brain cancer death associated with our Khamisiyah exposure data, by including each of these three smoke exposure indicators in the Cox model simultaneously with our Cox exposure variable. In each new model, with the added smoke exposure data, the risk of brain cancer death

associated with Khamisiyah remained unaltered. In other words, by adding additional exposure variable in it, original relationship didn't diminish, that relationship being between exposure and risk of brain cancer death.

The next slide please.

Among the study's findings were, there is a statistically significant increased risk of brain cancer death associated with modeled exposed to chemical warfare agents released at Khamisiyah among Army Gulf War Veterans. Secondly, as measured in the study, there is a dose, a pseudo-dose response relationship between exposure at Khamisiyah and risk of brain cancer death, where risk increased as length of exposure increased. And again, we know that the number of days exposed is just a surrogate measure of dosage.

The next slide please.

Additional analysis from this study included limiting our analysis to confirm primary brain cancer deaths did not effect the original findings. Secondly, a latency -- as latency increased, so did risk of brain cancer death among exposed. And finally, adding smoke exposure data to the model did not effect the original association we observed between Khamisiyah exposure and risk of brain cancer death.

Next slide please.

Among the study's limitations were lack of individual exposure estimates. This study only indicated whether or not the veteran was in the hazard area, and therefore had potential for exposure. Number of days in the hazard area again was only a surrogate measure of dosage. Secondly, exposures other than Sarin can not be ruled out as risk factors for the reported increased risk of brain cancer death. There may have been other -- there may have been chemical agents other than Sarin released at Khamisiyah. And finally, a multiple hypothesis testing may have lead to a spurious finding.

Next slide please.

There are certainly general accepted criteria for evaluating the association between exposure and an outcome. One is a temporal sequence, that is exposure predated the outcome, which in this case it appears it did. Secondly, is the strength association. This study reported a risk factor of almost three-fold for those exposed more than one day. Third, the grading effect, where the risk increases as exposure increase. Again, we saw the risk of brain cancer increased as length of exposure increased. Fourth, consistency of association across studies. To date, this is the only study that I know of that has reported an increased risk of brain cancer deaths among veterans exposed at Khamisiyah. And

finally five, which is related to that one, is biological plausibility. To date, animal studies have not indicated that neither Sarin or cyclosarin are carcinogens.

In fact, there is no indication that there was any even low level exposure on the battle field. There was not self reports of myosis or anything like that, which would be consistent with low level Sarin exposure.

Exposure that had been linked to brain cancers include exposure to ionizing radiation, electromagnetic waves and certain petrol/bio chemicals. We looked at the military occupational code of these guys and there was no clustering in any occupation that would have exposed them to any known risk factors for brain cancer. As a matter of fact, I believe it was 75, 80 percent of our study subjects of brain cancer, were in like a support position, or driving trucks or something like that. None of them were in the chemical warfare units or anything like that. They weren't in what you would think of as high risk occupations.

And finally, the times between exposure and associated outcome appears to be too short. This study only had a ten year follow-up period. So at the most, the time between exposure and death would have been ten years. And for many, as indicated in our latency

analysis, it was less than ten years. In general, the latency period between cancer induction and death is usually 15 to 25 years. Previous studies assessing risk of brain cancer due to environmental exposure have reported latency periods of 10 to 20 years. However, for some cancers, latency periods as short as two to five years have been reported.

The next slide please.

Finally, the findings in this study, while certainly not conclusive suggest the following additional research efforts: Continue to monitor the mortality of this cohort; examine geographical location of the brain cancer deaths, review exposure model for possible revisions, and finally, examine the effects of other risk factors in this cohort.

Thank you.

(Applause.)

DR. POLAND: Let's start off with questions, Mr. Bullman. Would you accept as one possible limitation also the idea that there was no difference in absolute types of primary cancer cell type between these --

DR. BULLMAN: Between the two groups, exactly.

DR. POLAND: Could you ask and maybe other speakers will have to answer. I'm not sure. In this

plume model, are you able to estimate possible level of concentration exposure versus those who work in the plants or others that would have been potentially exposed to --

DR. BULLMAN: I can't. Maybe someone else from OSA or Weber, who developed the model could.

DR. POLAND: Dr. Gray?

DR. GRAY: This is Greg Gray. We examined those data in two other papers previous to yours, and as I recall, they were very able, using the CHPPM data to model for the intensity of the exposure as well as the duration. I wonder, it's sort of strange here why you guys didn't use --

DR. BULLMAN: It wasn't available at the time we did our analysis. We strictly just had exposure, yes, no.

DR. GRAY: I would have to agree with Greg. That would be something to, not only to look at time, increasing time of exposure, but to look at the increase in intensity of the exposure. I think we had an exposure time, at least, in the second paper, which was authored by Tyler Smith.

Also in almost ever model we do for mortality or hospitalization risk or whatever, for the Gulf War Veterans, occupation has been very much an

important covariate. And again, one wonders, although you say that some of the people at greatest risk of some brain cancers were support people. One wondered about their petrol chemical exposures as a potential confounder. I know it is hard to get your arm around that, but occupational exposure has proven to be very important statistically in almost every outcome we've examined among the Gulf War Veterans, and it's rather easy to do using the DoD's Occupational Classification System.

DR. BULLMAN: I mentioned that we had look at the OSC and there was no difference between like brain cancer deaths, exposed or unexposed, regarding occupation. We also compared them to the larger group and there was no --

DR. GRAY: Did you use that in your model or did --

DR. BULLMAN: No, we didn't.

DR. GRAY: So you didn't use it in your model, but you simply looked at the cases. What I am suggesting is to use occupation in your model to see if you can identify specific occupations with an increased risk, and then follow that line of logic.

And finally you mentioned that you did multiple comparisons here and only showed us a table.

About how many different ICD-9 outcomes did you examine in your model.

DR. BULLMAN: In addition to looking at brain cancer, it looked at I think maybe 10 or 12 other specific cancer sites. As far as just causes other than cancer, we generally just looked at circulatory disease as a group. We looked at groupings rather than individual things. I think we also looked at ALS and some other diseases or causes of death that were at interest to Gulf War Veterans. But yes, we did look at others besides what was presented.

DR. GRAY: So would it be fair to say that you looked at dozens of outcomes and you found one or two that were significant?

DR. BULLMAN: Yes.

DR. GRAY: I think I'll just rest my discussion there.

DR. POLAND: Dr. Kaplan.

DR. KAPLAN: I am going to ask a very naive question. I guess it bothers me that we talk about brain cancer in this day and age when different tumors were listed in those that you had there. Is there -- has anybody looked at and I say it is a naive question, susceptibility or various tissues to this -- I mean you've showed three or four, as I recall on that slide,

different kinds of tumors. The term brain cancer seems to be a bit inclusive. Is that totally naive and off the board question?

MR. BULLMAN: Again, our data was based on death certificates, which were coded by Nosologists and then we picked out -- we chose those where the underlying cause was brain cancer. We requested their medical records and then we sent those and had those medical records evaluated by neurologist, I believe the paper cites who it was --

DR KAPLAN: What about pathologists, I mean --

DR. BULLMAN: No, no we didn't, no.

DR. HALPERIN: Bill Halperin. Vital status ascertainment was through about five years ago. What's the current status of --

DR. BULLMAN: We haven't updated the vital statistics on this group.

DR. HALPERIN: Okay, and you started accruing data on mortality when the soldiers left the field or when they left the site.

DR. BULLMAN: When they left the Gulf theater alive. I mean, the Gulf War was relatively -- Gulf I was a relatively short period, and these exposures occurred in '91 and I believe -- I mean, somebody may

know the number better than I. But I believe like 95, 96 percent of the troops left the theater around that date, I believe. So it -- yeah, our follow-up did begin the date they left alive. I think the dates are fairly close to exposure. I see what you're saying, but I am not sure there would be that much difference, in other words, if we began it the date of exposure or the date they left the theater.

DR. HALPERIN: Just one last question, when you compare the groups by length of exposure, are there differences between the groups, the one day, two day, three day --

DR. BULLMAN: Regarding other than mortality or -

DR. HALPERIN: Yes, industry and occupation, age, smoking, anything --

DR. BULLMAN: We don't have any smoking data. We don't have any occupations data except their MOSC, their job in the military while they were in the Gulf. No, we don't. We don't have any of that data.

DR. HALPERIN: Why would somebody be exposed for three days versus one day?

DR. BULLMAN: That -- I am not the best person to ask that, because I didn't design the model. But the model basically, you know, created a hazard area

over this four day period. I don't know if -- and it's based on like the company level, so the companies were moving in an out. Some companies maybe stayed in the hazard area. But the website that is associated with the Khamisiyah narrative, if it's cited in the paper, is very good. And it'll probably answer most of your questions about the model rather than me mistake something here about the model.

DR. LEDNAR: Wayne Lednar. A lot of our understanding of the toxicity of individual materials is looking at it in somewhat a pure form; for example, with some of the animal testing. The question I am wondering is, I am not familiar with this operation, but I would expect that in the process of taking out these sites, the actual agents might have in fact, had some combustion products. I am kind of wondering whether the toxicity of the combustion product is the same as the toxicity of the material if it were handled in the laboratory, and sort of a traditional toxicity testing. So the question is, has there been any modeling of what the products of combustion might be that would have, perhaps arisen during this operation, and then bring that back to the chamber here, and see whether or not there is any different toxicities that might involved --

DR. BULLMAN: It hasn't been done that I

know of, but yes, that would be something --

DR. GRAY: Let me jump in, this is Greg Gray again. Actually there were some tremendous modeling conducted at Aberdeen Proving Grounds to provide the basis for the first plume estimates. Some other individual may be more knowledgeable of that, but they actually did have mockups and surrogates for Sarin and appropriately sized casing and did some destruction modeling and looked at the residues, et cetera. Much of that information was fed into the first model and I'm sure used in the second model as well.

DR. BROWN: Mark Brown. I had in a previous job, somewhat dubious honor of going out to witness some of these experiments that were conducted by the Department of Defense out at Aberdeen Proving Ground where they tried to attempt to generate some storage terms that Greg was mentioning, generate some storage terms for the plume, this exposure. And it was interesting, they had created these crates, these wooden creates that contained these rockets, these short range rockets that contained Sarin and cyclosarin. And they piled them up, they stacked them according to the way they -- the best they understood they had been stacked at Khamisiyah, and set charges, or had the DoD guys that had done some of the original setting charges on these in

March of '91, when this event took place. And set off the charges.

I think the point is well taken that a lot of things were released from that. There was the combustion of blowing up these wooden crates and who knows. There was a lot of chemistry going on. It was not a clean experiment where you had a clean release of a single agent by any stretch of imagination. And I think Tim said that at one point. They modeled -- the Sarin exposure was the exposure of concern that generated this modeling. But it could just as well have been a surrogate for any number of items, such as combustion products from the wood or from the C4 explosives that were used. That would have gone up in this plume as well.

DR. PARKINSON: By admission I used to be the head of the Persian Gulf CCUP Program, on a tri-service team that put that all together. I remember when Khamisiyah was sprung on the IOM and others, you know -- Oh, I'm sorry, Mike Parkinson. The problem that I have always had, I just need an update on, you know, you could model whatever you want. Did we ever have any clinical experience of any acute or any biometric monitoring or anything of any potential nature that related people nearer to the site or proximal to the site as opposed to

downwind from the site, had any type of effect whatsoever? Did we go back and do anything more that -- I am dated in this, but was there ever anything that actually showed any human biologic, biomonitoring, any type of effect, related to anything related to Khamisiyah, either closer to where the destruction occurred as opposed to two, ten, 15, 180 miles away, that in any way validated the mere existence of the model.

DR. BULLMAN: No, not that I know of, but I might not be the best one. Maybe someone more experienced with the model or something. I'm not aware.

COL UNDERWOOD: This is COL Underwood. I am one of those statistics up there. I was one of the exposed individuals, but I would say at the time, we had no idea. I was with a medical company and there weren't increased visits or anything like that. So we were totally unaware of this.

DR. PARKINSON: I guess as part of the ongoing effort, is the model now taken as an accepted thing, it's kind of got -- is it undergoing anymore review or -- because it seems extremely -- at the time it seemed extremely controversial. Now it seems even more -- I mean, it just did not -- it defied clinical logic to say at the time that we couldn't find any even dose response, proximity, you know, near, distal to anything.

And I'm just looking for any validity information in the time since I left.

DR. BULLMAN: I believe that GAO actually conducted a review of the model several years ago, which we actually helped toward the end of the study. I believe that maybe, Dr. Brown, correct me if I am wrong, but I believe it was pretty much discredited or it's not longer being used. He could probably....

DR. BROWN: I'll add what I know about that. Two points, Mike. First of all, as you mentioned, the model was very controversial. It was reconstructing events that had occurred years in the past, so by it's very nature it was somewhat limited. And GAO, as Tim mentioned, did an analysis at the request of some members of congress about the quality of the model and basically, I'm not sure what GAOs standing as an organization that can evaluate that dispersion models, but nevertheless, that did not stop them from coming -- their conclusions were very critical and basically we had to sign -- VA had to sign a statement that we promise never to use that model again for research purposes. And the model is just a model. They used the best information they can try and assemble and tried to reconstruct what they thought might have happened, and that's with any model.

And the second point, as I understand

Department of Defense at the time, did -- there's other people who work with that organization, and I didn't -- but Department of Defense did what they -- so-called case narratives, where they evaluated certain events that were associated with the '91 Gulf War. They tried to think about the possible impacts on the health of service members who were there. And as I recall in the case narrative they did on Khamisiyah, one of the points that I think was important was that there were no descriptions of individuals showing clinical signs an symptoms of toxicity, of organophosphate agent toxicity, such as rhinorrhea, myosis and so forth.

There was not as I understand it and other people can comment on this, if anyone knows more about it, but there was not a single instance of an individual showing clinical signs and symptoms of poisoning. And that includes, for example, the actual DoD folks, the folks that were doing the planting of the charges on the rockets and blowing -- you know, the people who you might expect might have been at greatest risk, even in that group. Maybe somebody else can add to that.

DR. HALPERIN: I would like somebody to recount the early history of this study, if you will. Was there any indication there was a cluster of tumors in the population that was there; such that this cohort

mortality study might be documenting of a perceived cluster or were these a priority hypothesis --.

DR. BULLMAN: No, these weren't -- I mean, the last thing we expected going in an doing the mortality study was to find excess of brain cancer, brain tumors. We had no preconceived idea that that's what we'd find. Originally these studies -- It was not going to even include the mortality study. They were morbidity studies. They wanted to see if veterans who were notified of potential exposure, had more self-help or self-reported health problems than the veterans who weren't notified.

Then there was also going to be just a plain morbidity -- simple morbidity study looking at morbidity associated with exposure. And those are about to be published or have been published for military medicine. They essentially found there was no increased risk of brain cancer or brain tumors among people who were exposed. I mean, like I said. We didn't go in looking -- expecting brain tumors, but that's basically what we find, you know, when we don't -- to be responsible -- you know, report it.

DR. HALPERIN: With all due respect, you got involved through the IOM after this thing had a little momentum. Does anybody know the history when the idea of

doing the epi studies was generated. Was there any perception that there was a cluster of tumors?

DR. BROWN: Correct me if I am wrong, but I think -- wasn't the study originally paid for, commissioned by Department of Defense? As I understand it, the Department of Defense wanted an answer about what might have happened, what the health issues might be for those who were under this so-call plume, and they commissioned the department -- Institute of Medicine, who conducted the actual research. VA then got pulled in because we had access to certain data that was essential to conduct the study. But I think the original motivation, the original thought was -- came from DoD.

MS. EMBREY: I'm the director of the deployment health support, which is the successor organization to the Office of the Special Assistant to the Secretary of Defense for Gulf war Illness. And that office was engaged for a number of years in trying to address why they had unexplained illnesses and sponsored quite a number of research programs to understand the expanded claims of long term illness associated with the Gulf War service. I think what Dr. Brown said is exactly right.

I have a question on whether or not this study compared the rates of cancer to the general

population at the same age?

DR. BULLMAN: Yes, we did compare to the --

MS. EMBREY: What was that?

DR. BULLMAN: We calculated SMRs and we didn't present it here. And I don't even know if it was even in the journal article. I believe they were about the same. I don't think there were any increased risk. For all cancers or brain cancer?

MS. EMBREY: Brain cancer.

MR. BULLMAN: You know, without looking at that, I don't recall. I think there was an elevated -- increased. I know there was, as a matter of fact. There was an increased risk among exposed veterans compared to the U.S. general population. I don't recall how large it was, but there was an excess of brain cancer.

MS. EMBREY: My recollection is that it was minor?

DR. BULLMAN: It was -- You're right, but there was an increased risk.

DR. GRAY: I would like to call to the Board's attention that maybe eight years ago our predecessors were asked a question regarding this. I believe it was framed something like, if there were subclinical chronic manifestations of such an exposure, in other words, no acute manifestations at all, how would

they most likely be manifest and is it biologically plausible. I believe we used that document to frame some of our research, because they said peripheral neuropathies and things like that would be seen. I don't believe there was any indication for biological plausibility from such a phenomena as we are talking about here.

COL GIBSON: This is COL Gibson. You all will be getting a CD of literature reviews of Sarin. And in that is the AFEB report from '97, I believe it was.

DR. POLAND: Okay, Dr. Lednar, last comment before we move on to the next speaker.

DR. LEDNAR: Wayne Lednar. You mentioned that the brain cancer was not an apriori hypothesis going into this. From the toxicity of what is known about Sarin and some of the health effects, were any of those health effects that there is some toxicity and some biological plausibility of priority that's known, do any of those health outcomes show a higher than expected occurrence in follow-up in this group?

DR. BULLMAN: For like a respiratory disease or --

DR. LEDNAR: Anything?

DR. BULLMAN: No. Brain cancer -- that was about it.

DR POLAND: We'll move on now to our next speaker, Dr. Michelle Catlin.

(Applause.)

DR. POLAND: Dr. Catlin was the Study Director on the Institute of Medicine's updated literature review of Sarin published in 2004. On behalf of the Board, I thank her for coming here to update us on the current understanding of Sarin health effects. Her slides are right under the previous speaker's slides in Tab 2.

DR. CATLIN: I want to thank you for inviting me here to speak with you and tell you about our report. I'll start by giving -- I'm going to give a bit of a background on the National Academy of Sciences, and the Institute of Medicine for those of you who are not familiar with us.

Next slide please. I will then talk about our report, The Gulf War and Health: Updated Literature Review of Sarin. Then I will summarize at the end.

For those of you who are not familiar with the Institute of Medicine, which is a part of the National Academy of Sciences, we are a nonprofit independent advisory board, who was established back in 19 -- 1863, sorry, by President Lincoln. We are typically sought to advise on issues of sort of national consequences, a lot

of controversial issues within the government. When the government has a question that's very controversial, they'll turn to the National Academy of Sciences and the Institute of Medicine within that, to answer the question for them on scientific basis.

The reports that I work on including the Sarin report, for those reports, they are considered consensus reports for which we assemble on a committee of experts, expert volunteers, to address the issues, look at the scientific evidence and make conclusions. And those reports undergo a rigorous peer review process. For the Sarin report, we actually -- sorry, next slide. For the Sarin report we actually had -- there were six committee members, there was five reviewers who reviewed that report, and there is a coordinator who oversaw the review of the report to ensure that we had addressed all of the reviewer's comments.

I want to clarify the difference between the previous report that you heard about and the reports -- the consensus reports. The medical follow-up agency of the Institute of Medicine does conduct primary epidemiological research. Those are not consensus reports that are conducted by Institute of Medicine committees. The one I am talking about now is a consensus report, and there is a difference in the way

those are conducted and the types of questions that they answer, and the -- sort of the level of review they go through.

That said, I do know the one, the study by Bullman, it was reviewed by the Board that oversees the Medical Follow-Up Agency, which I believe Dr. Blazer is on, as well as the Board that did this one, the Updated Literature Review of Sarin. He's also a member of that Board.

Next slide please. To give you a little bit of background on Sarin, although many of you are probably familiar with this, Sarin and cyclosarin are chemical warfare agents that are members of the organophosphate compounds. And you've already heard everything else on this. I will point out at the bottom, that as you heard, there is no evidence from the time in Khamisiyah that there were actually any acute effects that you would typically see associated with an exposure to organophosphorus agents, including Sarin or cyclosarin.

Next slide please. With regard to this study, this study is part of a series of studies that have been conducted by the Intitute of Medicine, looking at the potential effects of various exposures that might have occurred during the Gulf War. Back in 1998, we were asked -- the Institute of Medicine was asked both by the

Department of Veterans Affairs to look at some of the potential long-term health effects of exposures that might have occurred in the Gulf War, as well as by two congressional mandates, telling the Veterans Affairs to come and ask us to do that. Because of these, we have convened a number of different committees to look at possible health effects of a number of the different agents that were potentially used in the Gulf War. These started with Volumes I, II, and III of Gulf War and Health. Those unlike the Sarin report which is nice and small, those ones resemble more like medical textbooks. They are huge probably a thousand pages, some of them; full size, hard cover books. We have reviewed everything from depleted uranium to pesticides and solvents, to the possible health effects of combustible products.

Back in Gulf War I, as we call it, the first of the volumes, we reviewed the literature on Sarin and the potential health effects of Sarin. Because of some new studies that came out following the release of Gulf War I, those studies were some toxicology studies that actually looked at the potential health effects in animals, of low level exposure to Sarin. The VA came back to us and asked us to update our literature review of Sarin and our conclusions of what the possible health effects of Sarin might be.

Next slide please. So when asked, we said, yes, we could do that. And we put together a committee of six experts. Everyone on here -- we have an epidemiologist, neurologist, toxicologist, to look at the question of what the potential health effects might be.

Next slide please. I have to show who the committee is, because they all volunteer their service, so we're very thankful for those people. The committee was charged to review the peer-reviewed literature published since the earlier IOM study, and to report on and make conclusions on the possible health effects of Sarin based on the updated literature as well as the preexisting literature that was reviewed in Gulf War I. We were not charged to determine whether or not the Gulf War Syndrome exists, nor to make any judgments as to the magnitudes of potential exposures. And as well, we were not charged to look at the broader issues, and we do not make any compensation conclusions or decisions or policy decisions. We just say what the science is and let the VA make the policy decisions on the basis of the science.

Next slide please. When approaching its charge, the committee began by having us do a data base search, and when we did the search, we reviewed -- retrieved and reviewed about 250 articles, both epidemiology articles and toxicology articles on Sarin

and cyclosarin. In general, the animal studies, when you have a good base on epi studies, the animal studies are generally used as supporting for the epi studies, but we do look at both the tox data and the epi data. And then we classify the evidence into five different categories that I'll tell you about later, but they are basically categories that are modeled on the IR category methods for epi studies, not the overall class I, AB, but the actual ones that they used for epi studies that are underlying that.

Next slide please. When we looked at the experimental animal data and the mechanistic data, one of the major drawbacks is that a lot of the studies that have been done, have looked at the acute effects -- they have been done at LD 50 doses looking at the acute toxicity, rather than looking at what the possible effects could be of low level exposures. So we had to -- when we were looking at all of the evidence, we had to separate out the effects of -- what I'll call high level exposure, that causes an acute cholinergic syndrome, which is typically seen with high level exposures to organophosphate compounds, and what might occur with low level exposures. The reason we separate them out like this, is because as I said, there was no evidence that anyone in the Gulf War was exposed to levels that caused

the acute cholinergic syndrome. There are a lot of sort of sequela of the acute cholinergic syndrome that are seen so we wanted to make sure we differentiated between the effects seen at a high concentration and at a low concentration. When we looked at those studies that -- I'm sorry. I'll back up.

With the acute toxicity, the principal mechanism of that toxicity is thought to be inhibition of an enzyme, acetylcholine esterase enzyme, and you get obvious sign of about 70 percent inhibition of that enzyme. That mechanism is pretty well established for all organophosphoric compounds. When you look at any potential effects that could be resulting from a lower level of exposure, it's not known what the mechanism would be for that, so we have to sort of look at the mechanism separately as well for the two different types of exposures.

Next slide please. As I mentioned, the effects of high level exposure are fairly well established, so we were very concerned with what was going on at low level exposures, especially in light of the new animal studies that were sort of the impetus for doing this study in the first place. When we looked at the animal data that were available from low dose exposures, there are some new data that came out, and

there are some results that were showing up in these studies as possible effects of low level exposure. There is some behavioral effects done, behavioral studies done. There were some effects on local motor activity in rats that were seen. And they looked -- however they looked at local motor activity or behavioral activity with exposures to Sarin as well as with exposures to high temperatures and the mixture of the two. So they saw some effects but there were sort of no consistent behavioral effects that were seen just on the basis of Sarin exposure in those studies. They also did histopathology on the rats 30 days after exposure, so they actually had a cessation of exposure so that you could look and say, okay, we exposed the rats to a low dose of Sarin, you stop the exposure, you let the rats go for -- live for another month or two, and then you look and see what the effects were with that cessation of exposure built in. Thirty days after the exposure there were no lesions seen in the brain and no evidence of cell death. There was no consistent effect on total brain acetylcholine esterase measurements. There were, however, in some areas, decreased levels of that enzyme. There were changes in some of the brain's cytokine concentrations that were affected both by Sarin and by heat stress. And as well, in certain regions of the

brain, there were changes in the density of some of the muscarinic receptors, which is the receptor subtype that Sarin would act upon.

When we looked at the overall body of the tox data though, and especially the receptor density results, although it suggests the potential mechanism that some long term effects could be caused by, there was no way to link this up to any sort of an effect in humans. There is no way to say this changes a muscarinic receptor density would cause or could be associated with brain tumors or any disease, Parkinson's, Alzheimer's. It just wasn't known what possible health outcome you can draw on the basis of those studies.

Next slide. In addition, as I said, there is some behavioral effects. There is some studies done in mazes, looking at exposure to Sarin as well as Sarin plus oximes. Once again, there were some affects but most of these effects were reversed three months out, and it wasn't sort of consistent enough to draw any strong conclusions on. There was also some immune effects, once again not overly consistent, and I do want to point out in light of the question to the Board about brain cancer; in general, the genotoxicity studies that have been conducted with Sarin have been negative. There has been one study in rats that showed an increased in unscheduled

DNA repair, but there was some problems with the controls in that study, and other studies have not shown any DNA effects.

When it comes to looking at the chronic animal studies to try and look for cancer, there is no evidence of cancer, however the proper studies have not been conducted to be able to draw any conclusions on the basis of that. There have been no chronic carcinogenicity studies in animals to date.

Next slide please. We then switch to look at what epidemiology studies were out there. When looking at the epi studies, the studies can typically be broken down into four different categories. The first are studies that were conducted in military volunteers who were exposed to several chemical warfare agents, both in the US and in the UK. The second are industrial workers who have been studied. The third are victims of Sarin terrorist attacks that occurred in Japan. And the fourth are studies that have been conducted in Gulf War Veterans.

The first three of these, all studies that have been conducted to date, have been conducted on people who showed signs or symptoms of the acute cholinergic syndrome. So any conclusions that can be drawn on the basis of those data, must be drawn on people

who had elevated, higher exposures to Sarin or cyclosarin, because they were exhibiting the acute cholinergic syndrome.

The fourth, the Gulf War Veterans do have data on people who were exposed at lower -- potentially exposed at lower concentrations. So I will talk about those. I want to point out that our study was concluded prior to the publication of Dr. Bullman's study, so the conclusions of that study are not included in our review. We actually -- when we were doing our study, we knew that that other study was going on, that Dr. Bullman's study was going on. We had tried to delay our report waiting to get the results of that so we could include that in our report and in our analysis, but the timing wasn't quite right, so we had to go ahead and publish, because people wanted our study out there.

Next slide please. We then looked at the body of epi literature and we broke it down looking at what studies had looked at different types of health outcomes. So the rest of my talk, we'll talk about neurological effects that might be seen, cardiovascular effects that might be seen, and any other effects that might have actually been seen in some of the studies.

Most of the studies do focus on neurologic effects, because Sarin is a neurological -- neurotoxin,

so that was the focus of many of the studies, was looking at possible neurological effects. When you looked at the studies of military volunteers, there did not -- there was not any demonstration of any long term health affects, following the exposure to cholinesterase inhibitors. In that as I said, some of the subjects did experience acute cholinergic syndrome, but it still is not known what the concentrations actually were in those subjects. Those subjects have been followed ten years out and 25 years out. But they did not look at cancers in any of those studies that they did.

When they looked at industrial workers, there were some EEG effects seen, but the clinical significance of those effects remain unknown. The workers that were studied had actually they classified the workers in those studies as exposed on the basis of having exhibited signs and symptoms of acute cholinergic syndrome.

And when looking at the victims of the Sarin attacks, those Sarin attacks occurred back in '94 or '95, so the furtherest out follow-up is probably less than ten years right now, as far as follow-up on those subjects. There have been evidence in those subjects of persistent fatigue, headaches, memory loss, visual disturbances, however all of those effects have been seen in people who, you know, by classification, are the victims were

those who exhibited the acute cholinergic syndrome. So they're useful for drawing conclusions on possible long term effects following high dose exposure, but not for following chronic low dose exposure or even just short period low dose exposure.

Next slide please. When we looked at the volume of literature on the Gulf War Veterans, we separated out, because we were looking at the effects of Sarin, we separated out the literature into the literature on those who are potentially exposed at Khamisiyah to Sarin and then the other studies. When looking at those potentially exposed at Khamisiyah, there were four studies that have been conducted, that we reviewed in our report. In those studies, there were no differences that were found between troops who were and who were not present at Khamisiyah. I should add that all of these studies used various versions of the models that you've heard about, depending on when the study was published, it basically used the most up to date model, which started with, I think it was a 50 kilometer radius from Khamisiyah, point, that was the initial troops that were notified that they might have been exposed to Sarin, was anyone within a 50 kilometer radius of Khamisiyah. And they then upgraded that model to start including some of the meteorological effects and where the plume might

have actually been going. So as the model evolved, the epi studies have used the more evolved models. But I don't go into the details as to which studies used which models. But exposure assessment in these studies is a large limitation.

So when we looked at those who are potentially exposed at Khamisiyah by their presence there, there were no differences seen between those exposed and those not exposed. When you broke it out and a lot of studies break things down at to whether or not they witnessed the explosion or whether or not they reported having been there, eight years after the exposure or the explosion, those who reported witnessing the explosion were more likely to have self-reported changes in memory, difficulty in sleeping, persistent fatigue and depression. But as I said, there is a lot of uncertainties when you look at the exposure modeling in these studies.

Next slide please. The other types of exposures of the reports that we looked at all had self-reported exposures, and we can well imagine, if you're sitting in a room with a lot of epidemiologists, this was a large limitation in their mind to these studies. In these you had self-reports that might have said exposure to chemical warfare agents. Basically they

look at potential health affects in different groups of people and they have questionnaires for those people as to what their exposure might have been. And these can run the gamut from chemical warfare agents through putting on chemical warfare suits, hearing alarms, and then everything through gasoline, you name the exposure that could have happened in the Gulf. It's on the list of potential exposures in these studies. And they look at all the potential exposures, a number of different health outcomes, sometimes clustered into syndromes that they've defined, and look for any associations.

Some of the people who self-reported that they were exposed to chemical warfare agents, there were some associated neurological findings in those individuals. In other studies there were no effects seen. Whether it was self-reported nerve gas agent or hearing chemical alarms or putting on an NBC suit. So when you looked at the overall effects and the neurological effects in these groups of people, there was no consistent effect that could be linked to Sarin. You have to remember when we are doing these studies, we are looking specifically at possible health effects of Sarin. So everything is going back to whether or not A is linked to -- even the exposure that they are having as sort of a surrogate for Sarin, or then you have to go, okay, is

that surrogate actually valid as a surrogate for Sarin exposure. Even when you looked at the surrogates of Sarin, there is no consistent effect seen across all the different epi studies.

Next slide please. When you looked at posttraumatic stress disorder, PTSD was seen in survivors of the Tokyo and Matsumoto Sarin attacks. And in British veterans who reported either wearing nuclear biological and chemical warfare suits, or hearing chemical alarms or having a chemical nerve gas attack. There were other studies that did not find a relationship between PTSD and some of the indicators of Sarin -- or surrogates of Sarin, I should say. And PTSD was not more common along those who were thought, based on the modeling to be exposed at Khamisiyah and nonexposed Gulf War Veterans. One of the big limitations with the PTSD studies, when trying to link it to an actual chemical exposure, is you don't know whether PTSD would even be caused by the chemical itself, or by the traumatic event that was occurring around the chemical exposure.

Next slide please. There have also been some reports of persistent cardiovascular effects following exposure to Sarin. These cardiovascular effects have been evident in some studies of the victims of the Tokyo attack, and as well, one study of personnel deployed

during the time of Khamisiyah, did find one cardiac dysrhythmia -- sorry, one effect for that -- one cardiovascular effect, that being cardiac dysrhythmia, out of ten cardiovascular effects that were seen. Other studies showed cardiovascular effects but only when they looked at deployed versus nondeployed. These studies that were done on Gulf War Veterans were actually very hard to sort of dissect through, because they will compare Khamisiyah versus non Khamisiyah, deployed versus nondeployed. So there is a lot of different comparisons going on, so you have to really watch what is being compared when, when you're drawing conclusions.

Next slide. As well, there have been other health effects that have been studied. I mentioned, a lot of these studies look at multisymptom illness or clusters of symptoms that they link into a syndrome. There has been a case of Gulf War illness associated with the use of gas masks. Also responding yes to thought biological or chemical weapons were being used. That was linked up with multisymptom illness. A number of these are looking at multisymptom illness, chronic fatigue syndrome, PTSD, and these different syndromes. There have actually been studies that show an increase prevalence, mostly with deployment, not necessarily with any surrogate for Sarin exposure.

Once again in those studies, exposure assessment is not very reliable indicator of actual exposures. In addition, in some of those studies, the medical symptoms are actually self-report as well. So that even calls the question, even more, as to what you have and the conclusions you can draw on the basis of those studies.

I will add, most of these studies were conducted within ten years, finished within ten years of the Gulf War, so most of these studies did not even look at cancer.

Next slide please. When the committee went to draw conclusions, they made conclusions based on the scientific data and they classified as I said, into five different categories. Those categories have been -- they are based on the IR categories and they have been used in a number of previous IOM studies, slightly modified at times. They are the categories that were used for the other Gulf War and Health Studies. They have also been used for IOM's safety series of reports, as well as the Veterans and Agent Orange reports that look at the potential effects of herbicides used in Viet Nam.

Next slide please. The five categories of evidence and you're not going to be able to read these, but you can read them in our reports if you ever want to

see them. We made conclusions as to whether there is sufficient evidence of a causal relationship between a given agent and a given health outcome; whether there is sufficient evidence of an association, limited suggestive evidence of an association, inadequate or insufficient evidence to determine whether or not an association exists, and limited suggestive evidence of no association.

So the committees basically go through and look at the evidence and draw conclusions on the different health outcomes and place them into one of these five categories of evidence. In practice, when we're looking especially for the Gulf War reports at numerous, numerous chemicals in some of these cases, solvents and pesticides, probably reviewed about 50 different chemicals at least. We only draw conclusions, state the conclusion when there is even any research done on that, whatsoever, because we can't go through a laundry list of every health outcome and plunk it in there, but if it has been looked at, we will draw a conclusion and place it in one of the five categories of evidence.

Next slide. The committee did conclude that there is sufficient evidence of a causal relationship between exposure to Sarin and the acute cholinergic

syndrome. This is not rocket science here. This is nothing new.

Next slide. Based on the evidence from the epi studies that are available and the supporting evidence from animals, the committee did conclude that there is limited suggested evidence of an association between exposure to Sarin or cyclosarin in doses that cause the acute cholinergic syndrome and a variety of subsequent long term neurological effects. So if you have acute cholinergic syndrome, there is the possibility that there will be long term effects following that syndrome. This is also something all that new.

Next slide. When looking at persistent neurological effects following low level exposure, so in the absence of any signs or symptoms of the acute cholinergic syndrome, the committee did conclude that there is insufficient evidence to determine whether or not there is an association between low level exposure to Sarin and any subsequent neurological effects long term.

Next slide. When it looked at the cardiovascular effects although there are starting to be some data that shows some effects following high dose exposure to Sarin, when it comes to low level exposure, there is inadequate or insufficient evidence to conclude that there are any long term effects.

Next slide. And that was the other health outcomes I had talked about, there wasn't even enough data to draw any sort of real conclusions about that whatsoever.

So basically in summary, there are sufficient enough data to show that the acute cholinergic syndrome exists following Sarin exposure and that there might be some long term sequela of that syndrome, but given the few epidemiology studies and the limitations especially of those studies that do exist, and the limited number of relative toxicology studies, there are inadequate and insufficient data to determine whether or not any long term effects would occur following exposure to low level Sarin.

Thank you.

DR. POLAND: We have about three or four minutes for questions from the Board.

DR. LEDNAR: Wayne Lednar, thank you for that, it's really very helpful. As you look at the kinds of individuals who were included in the studies that show at low doses, where you can see cholinergic effects, some of the follow-up for neurologic signs, you think of those kinds of people who are in those studies, and then compared to the kinds of people who are on the ground at Khamisiyah, is there any reason to think that the types

of people that we are trying to answer the question around are healthier, more fit, in some way less vulnerable to having some of the acute effects that are seen on exposure, from the literature?

DR. CATLIN: I have never really thought about that, but given some of the studies, one study was with the acute effects that we looked at military volunteers. So I would say those population would be very similar to what was on the ground in Iraq and in Khamisiyah. The industrial workers, I mean, you do have the healthy worker effect, where the workers would be healthy if they're out working, but I would not know anything and there would not be any data. I mean, when you start getting into the military volunteers and the industrial workers in these studies, the studies are very old and not very vigorous.

The Sarin attacks in Japan, they would be just your typical generic population, because one was in a residential neighborhood, and the other was on a subway system in Tokyo. So there could be a possibility that that the military would have healthier people than the generally population of Japan, but I would have no idea. I don't know what the general health status of Japan versus the U.S. military is.

DR. LAUDER: Just a question of

clarification, going back to Khamisiyah. I'm sorry, Dr. Tamara Lauder. Did you state earlier that those subjects that had brain tumors did not have any evidence of acute cholinergic symptoms?

DR. CATLIN: There is no evidence that anyone in the Gulf War had any acute cholinergic symptoms. And that's based on both self-reports, like medical surveys that were sent to them and asking them about different symptoms, signs and symptoms. There was no evidence from those. But as you mentioned, there is no reports while over there of anyone seeking medical attention.

DR. LAUDER: Hence an indirect answer to some sort of exposure level?

DR. CATLIN: Yeah, there's no signs that the exposures were high enough to provide acute cholinergic syndrome, unless as the other person pointed out, for some reason the military is less susceptible. It was also, I should point out at Khamisiyah, from what we've read, there were no chemical alarms going off and they never thought that there were chemical weapons down there, so no one was actually wearing gas masks or anything, and even NBC from what I understand.

COL UNDERWOOD: That is correct. This is COL Underwood.

DR. SILVA: Joe Silva. Thank you for the

nice reviews. How many drugs are out there that cause in animals brain tumors. I mean, most of our chemically driven carcinogenic events are long term exposure, with the exception of some types of radiation.

DR. CATLIN: We looked to see and there -- like you say, radiation was one of the main things. There's not a whole lot known as to the etiology of a lot of brain cancers. There just isn't a lot known about it. We also looked to see with the organophosphate compounds. And this review came after a previous textbook on solvents and pesticides that we produced. And with all of the organophosphate compounds, there was no indication of brain cancer. There were some cancers, but not brain cancer seen following exposure to organophosphate compounds. I can't remember the details and the provisions on that. We have them there if you want. So we've looked at sort of the organophosphate compounds which you would think might have had a similar effect, and we couldn't find anything. And there is nothing to link up even the animal data, the changes in muscarinic receptors, we looked to see if those particular types of changes might be linked up to other outcomes, and to be honest, we actually did look carefully at brain cancer, because we knew this study was coming out, and there was nothing that we could find that

would show that at least published at the time.

CPT JOHNSTON: You mentioned in one of your earlier slides that not all the effects of Sarin appear to be due to acetylcholine esterase inhibition. What other affects did Sarin have?

DR. CATLIN: That's a good question. I can't remember now. It has been a few years since I did the study. It is more with Sarin, organophosphate compound when you start getting into low levels. Some of the effects just don't seem to correlate with the changes in acetylcholine esterase enzymes, and I honestly can't remember now what they are. Sorry.

DR. PARKINSON: Perhaps on a lighter note, I'm not going to profess to understand the increase in unscheduled DNA repair means, I can't remember the last time I got my DNA scheduled to be repaired.

The second thing is that the rat (laughter) -- the second is the rat performance in the maze was quote, "somewhat effective." What else are the poor rats supposed to do. In all seriousness, are you saying that the conclusions of the committee, looking at the animal studies were at best inconclusive, and maybe even meaningless?

DR. CATLIN: I wouldn't say meaningless. I would say when you're starting to try and extrapolate

from the animal data to the human, it's just not there. It's too inconclusive to extrapolate. What they did say, based on the animal studies, especially what was going on with the receptor density and such, that this is something that should be looked at more in animals. Because it's an interesting finding, it's a hypothesis of something other than strictly acetylcholine esterase inhibition that could be going on with low level exposure, so it's worth looking at. But it's not strong enough and it's inconclusive when trying to draw anything above a human outcome, or even a rat outcome. You couldn't even -- given what data were there, you could not say it caused -- Sarin causes hyperactivity in rats. It just wasn't a strong enough study with only one study showing it. Does that answer your question?

DR. LAUDER: I have one more question and it may be directed to Dr. Bullman or perhaps Dr. Catlin. I just wanted to know if when you broke down the types of brain tumors that you looked at, you had Astrocytoma, Oligodendroglioma, and you broke that down into years of three; three, six, and nine. Were you able to break down the types of tumors within each of those segments.

DR. BULLMAN: No actually, you mean the latency analysis?

DR. POLAND: Basicly did you see different

histology over time?

DR. BULLMAN: Oh, regarding the specific cell types. No, we didn't look at that. The only thing we did the latency analysis, we did the latency analysis with all brain cancers. All 52 or 55. It wasn't limited to a specific cell type or primary versus others.

DR. LAUDER: Can you do that?

DR. BULLMAN: Yes, we could.

DR. LAUDER: Because I think it depends upon a cell type how fast growing it is. If you see a cell type the first three years, and it is not that fast growing, it therefore could not be associated with what perhaps you're trying to associate --

DR. BULLMAN: That's one of the things I mentioned in the study. It was just a very short latency period, much shorter than what you would expect for most cancers. It was ten years at the most, what we had. And I believe in most cancer between exposure and death, 15 to 25, 15 to 20 or something like that, so that's outside below the rate. But yes, that is something we could do.

DR. LEMASTERS: Grace Lemasters. Don't go away. I don't know who is the best person to answer this. I was wondering if you did any kind of lag analysis requiring -- I have two questions, minimal amount of lag time before the occurrence of cancer, and

the second question is related to that is what is the normal latency period for brain cancers? And then just a third quick question, could you apply the information about those who witnessed the explosion to the mortality? Do you know in your mortality analysis, the data that's available about witnessing the explosion?

DR. BULLMAN: I will answer your last question first. No, we didn't have that kind of data.

DR. LEMASTERS: Can you apply it?

DR. BULLMAN: If we had the data, yeah. And regarding the lag analysis or latency analysis, are you wanting to know when was the earliest tumor, when did that occur?

DR. LEMASTERS: Yeah.

DR. BULLMAN: I don't have the follow-up here in front of me. I believe, let me see. Most of them, that's '91 follow-up. Those started in 1991. I don't want to answer it, because I am not sure. I can't say offhand.

DR. LEMASTERS: I know you both reviewed about brain cancer. What is the average latency period was the third question?

MR. BULLMAN: About 15 to 25 -- I believe it is like 15 to 25 years, and outside of the range, like I said. The most we had was a ten year follow-up, '91 to

2000. The latency period between exposure and death by brain cancer, I believe is -- somebody else, if they know the right answer, feel free to correct me, I believe it's like 15 to 20, or 15 to 25, something like that.

DR. POLAND: We are going to need to stop or we'll just get too far off track. Thank you both and we will break for 15 minutes and then reconvene.

(Break at 10:09 a.m. to 10:32 a.m.)

COL GIBSON: This is a list for taxis for tomorrow for people who want to take a taxi back to the airport. That list is going around, so you can sign your name if you need a taxi for tomorrow. We'd greatly appreciate it. The other thing is, we have a few of the Armed Forces Epi Board History and Commission Books. They're hard bound books back here on this back table. We got a republication of that whole series of books and I've got a bunch of them back at the office. I brought a few of them here. They're free. Please feel free to take one if you like.

DR. POLAND: We'll have to update that history some day. Okay, I want to keep us trying to move along. Our next speaker is Mr. Cushen, Chief of Occupational Health in the Risk Management Directorate of the US Army Chemical Materials Agency at Aberdeen Proving Grounds. He'll provide us with the Army Occupational and

Environmental Protection Program for Destruction of Chemical Munitions. Thank you.

MR. CUSHEN: Thank you. Next slide please. Our mission for occupational health with the Chemical Materials Agency is to medically support the safe destruction and dispose of chemical munitions. Currently today we have three incinerator sites operating burning Sarin. And we have one neutralization site neutralizing VX which is also organophosphate. So this is -- the daily application of this problem is a huge undertaking for us. We also want to preserve and prevent the occurrence of occupational disease and injuries in our work places, and provide the highest quality occupational health services to our workers.

Next slide. To do that, we have numerous program elements. Medical survellience which includes biological monitoring. Personal Reliability Program Screening. We don't let just anybody come into our sites and handle chemical weapons. They have to be screened for drug use, alcohol dependency. It's very hard to get in the program. It's very easy to get removed.

We also do substance abuse and prevention. We have emergency medical response service. If there is an accident in one of our plants, we need to be able to take care of those casualties very quickly. Our goal is

to have then to medical care within four minutes. The main reason is, when you get a large dose of nerve agent, the first thing that shuts down is breathing. Without oxygen, life is not good.

We also do treatment of minor illnesses and injuries on the job. A lot of worker health education and training, and health promotion as time permits. Most of our work force in the demil plants are contractors, and our storage site, they're all government civilians. We did a demographic look at our work force. They are older. They have high blood pressure, and they -- at a lot of places are fairly overweight. We have one person that is under 21. We have several that are over 72. Most of them fall in the 50, late 40's to 60 age range. It is an aging work force.

Next slide please. Our Medical Surveillance Program. We establish a baseline of health. We do that through an initial interview, when they are put into the Personnel Reliability Program. They have a physical and a baseline established then. And we do an annual update of their health. Cardiovascular health is very important, hearing, substance abuse, random drug screen. Everything we can do to ensure that we have a reliable work force to handle weapons.

We also look for early detection of

subclinical workplace exposures, trying to reverse, halt, or retard disease progression. Not only for agents but also for other industrial hazards. We do an evaluation of worker fitness for essential job functions, including respirator and audiometric [sic - audiologic] testing. We do an assessment of worker protection afforded by engineering controls. Our plants have four levels of control. We have level A, where we know there agent present, and you cannot go in there unless you were in an OSHA suit and you're limited to a two hour stay time. We have level B areas, which is basically outside of the level A. And there you have to be in SCBA, self-contained breathing apparatus. Outside -- it's a tier effect. Outside of that is level C, where we have lesser air purifying respirators as respiratory protection. And level D is everything outside the plant. When you come -- if you come to one of our plants, the first thing you do before you get near the plant is you're issued an M40 mask, an air purifying respirator, so in case there is an accident, and we have an alarm, you can mask and safely egress. Again, worker safety and protection of our workers, our visitors, and the populous, the population around our plants are very important.

We also do biological monitoring for heat stressful entries. We put men and women every day in a

self-enclosed suit for two hours and send them into hot areas of the plant where it can be 90 plus degrees. Before we do that, we screen them medically, blood pressure, urine specific gravity, because we're looking to make sure we don't cause a heat injury while we protect them.

Next slide please. We have a health hazard inventory because we have incinerator and neutralization plants, there're industrial areas. They're dangerous. When we do maintenance that's generally our most dangerous time. We list all of the physical and chemical hazards. We key it toward the workplace and make sure workers are aware. We do job hazard analysis for each operation we do. We also have detailed SOPs that go through step by step, the sequence of events that is going to happen, so that everyone knows what is going to happen next. Again, to minimize chance for accidents.

We identify personnel who are exposed, and we qualify those in relation to the airborne exposure limits. We look at the short term exposure limit or STEL, the worker protection limit or WPL, which -- excuse me. The STEL is a 15 minute time weighted average, concentration and time. The WPL is an eight hour time weighted average. And the IDLH is an instantaneous reading that is immediately dangerous to life and health.

These all form the basis for our medical surveillance exam.

Next slide please. Our Heat Strain Control Program, again, when we put -- we have incinerators that burn toxic agents at 2000 degrees. It's a heat stressful environment. We know that. We monitor for that. And we do things to mitigate that risk to our workers. Again, we do pre-entry screening to make sure that people are medically and physiologically prepared to go into a heat stressful environment. Because if someone goes down in our plant, it affects -- it affects them. It's also the rescue effort to get them out is burdensome because we then have to put more people into hazardous environments to extract them. We have baseline screening and enrollment medical surveillance for heat strain. We do physiological monitoring for all encapsulating entries, both pre and post entry. And if they don't screen, if they don't pass a pre-screening, they are turned away. If it is for hydration, they go back and they rehydrate and they come back and are rescreened. Or if their blood pressure is wrong, they are referred to their supervisor.

We have established criteria for precluding or terminating heat stressful entries. As we have -- in our control rooms we place a paramedic in a control room. And every 15 minutes, we use heart rate to approximate

heat load. Every 15 minutes the paramedic asks the person in the entry to turn toward the camera and they read their heart rate. And the paramedic has pre-screened them and knows when they approach a certain value, they need to either sit down and rest, or if they rest and their heart rate does not come down, they terminate the entry and we send another crew in to finish the job.

Next slide. Personnel Reliability Program Screening. We review the history, their medical records, their exams and referrals. We look for information that's potentially disqualifying. Do they have a history of fainting, do they have a history of high blood pressure, do they have uncontrolled diabetes. Do they have a history of drug use. All of these things again trying to come up -- have workers that we can have handle our chemical weapons that are reliable and have no disqualifying information. They are recommended for selection and retention in the program and if they have something as they come up, if they have a new onset of diabetes, and it is uncontrolled, they need to be either temporarily or permanently disqualified. If there is drug use in one of the random drug screens, they are permanently disqualified.

Next slide please. Our Substance Abuse

Program, we look for signs of abuse and dependency. We do a hundred percent urine drug screening for our chemical work force. We do random alcohol testing, random breath alcohol testing. Again, when we do a prescreening to go into one of our either demil or storage sites, alcohol is a predisposer for heat injuries, so we look at it from both a reliability standpoint as well as being predisposed to a heat injury.

We have a medical review officer that makes the final determination and then at the end, we refer them for appropriate treatment.

Next slide. Advance Medical Care and Emergency Response. Again, if someone is injured in one of our plants and they have been working with agent, the hospitals downtown do not want them. They want them clean. They do not want a contamination hazard showing up. There's a program called SECEP, that interacts with the hospitals. The hospitals that support our plants have decon capability. They have special training for their emergency departments to handle contaminated casualties. But our goal is to give them clean casualties. We have ACLS capabilities at our clinics. We have decon capability in the plant. Because of the effects Sarin especially on the breathing system, we have to get them to medical care as quickly as we can. We say

we'd rather have a contaminated casualty than a clean corpse. So we decon as best we can, but we don't want them so clean that they die because -- if we take ten minutes to decon someone and they're not breathing, it doesn't do them any good. It's hard, because everyone is like, we've got to keep the agent inside. Engineering controls, but where we need to, we do if we have to -- we have capability, all of our clinics at the demil plants and the storage depots have a decon room where they can bring people in and decon them while medical care is ongoing.

Once the casualties are stabilized they are treated and transported off site. We have no holding capability. Our goal is to decontaminate, resuscitate, and transport.

Local hospitals again, they have training in caring for nerve agent casualties sponsored by the SECEP program, and we also have support, if there is a large incident, where different experts from the Army would go to the site and provide guidance.

We also do treatment of minor illnesses and nonchemical related injury. That's because by the time you get through the process to get into our plants or to our storage site, because they're remotely located, it is more cost effective to treat minor things there than send

them to their own physicians.

We have inadvertently exposed people to nerve agent and had cholinesterase suppression.

Next slide. This is a typical -- we establish a baseline of cholinesterase. Everyone's baseline is very independent of them. We monitor that over time, and in this instance, there is a significant exposure and as you can see, a significant depression. But their baseline did over time return to normal, and this patient continues to work in the program.

Next slide. When we do -- generally about once a month an alarm goes off and people aren't in the right protective gear, and we have to do potential exposure evaluations, where we look for cholinesterase as well as other indicators. It is conducted whenever we exceed the airborne exposure limit or established thresholds of dermal or inhalation toxicity. It includes a medical exam and confirmation assays, including if we have a depression in cholinesterase or a known mustard, we have an agreement with CDC and the Medical Institute for Chemical Defense At Edgewood, it's an Army lab, to look at metabolites, to go back and see -- to confirm the exposure.

Next slide. Employee Medical Recordkeeping. This is probably -- for our physicians, this is probably

one of the harder things. Their occupational records, their Army records or a contractor's that has monitoring data for both nonagent and agent related exposures or physical hazards, and they are maintained in accordance with 29 CFR 1910.120 for their employment period plus 30 years.

Next slide. I have talked about our exposure limits. These units are in milligrams per cubic meter. At the bottom you can see what the immediately dangerous to life and health is, and then the STEL is a short term exposure limit. The WPL is a workplace worker protection limit. The GPL is a 12 hour limit, and that is for the general population that is outside the fence of our installation. All of these limits were recently revised and implemented last January, for agents GA/GB, and VX. Mustard followed in July.

The CDC when they published these limits in the federal register, said what we do is protective, however our practice -- we treated at AR time weighted average as a short term limit. And in theory, we had an eight hour limit that we used as an instantaneous limit, and so they went back and changed the exposure limits based on that information. So our old eight hour limit became our new 15 minute limit and we have taken that probably a step further and we monitor -- I will talk

about monitoring in a minutes.

We monitor at a fraction of the short term exposure limit using near real time monitors. We monitor for a period of three, five or ten minutes and analyze, and if the alarm goes off based on that monitoring, we either put people in protective masks, or if they are in appropriate equipment, we just know and annotate that the alarms went off. But if the people aren't in appropriate protective gear, they come out of the area they are in, it is upgraded from the category D to a category C, or C to B, and we send any potentially exposed workers to the health clinic for post exposure follow-up.

Next slide please. This is our risk management approach. We use air monitoring extensively to verify other components of a total risk management system. We have engineering controls, sealed rooms, cascade air filtration which are described as the AB, level A, level B, level C, and level D categories of our plants. We have negative pressure. Most negative pressure is in level A. Goes out from there. All of our air from our plants is run through carbon filters before it's released. We monitor mid bed of the carbon filter to ensure that we're not releasing agent to the atmosphere. And because we process loaded munitions, we have explosive containment rooms within our plants that

have thick concrete walls that will contain -- if a round explodes, it will contain the explosion and we won't release agent to the atmosphere. One other thing -- the plants were designed, that was a critical piece. What is the biggest explosion you could have, and engineered a solution above and beyond that, so if something does happen, again we contain all of the agent inside the plant. And we don't expose our workers or the public. Our work practices, training, lessons learned as well as surveillance. Our surveillance, we go in on a routine basis to all of the igloos where munitions are stored and check for leakers. If we find something that's leaking, we bring back appropriately suited people, workers and repalletize, recontainerize, and put the leaking or suspected leaking munitions and overpack containers and then put them in cycle to be destroyed in demil process.

Next slide. This is the what our OSHA level A looks like. It is called a demilitarization protective ensemble. It is strictly -- it was developed for the chemical demil program. It covers head to toe, and it's totally encapsulating and the back of it is heat sealed, and it is over pressured.

Next slide. This is our OSHA level B. Again, totally encapsulated. OSHA A is vapor tight. OSHA B is not. This has SCBA with is supplied air worn

on the back. We use this if there's a problem with one of our level A entries. We have people -- have people ready in level B to go in and do the rescue.

Next slide. This is a level C. This is what we mainly use when we are going into a storage igloo and to do surveillance. We send people in in this. It is not vapor tight. If they have liquid on them, they are potentially exposed. It is hot. It is butyl rubber. It hangs on you and the heat load from this, you don't like to wear it.

Next slide. Our monitoring, again, every plant especially the demil is being monitored 24 hours a day, seven days a week at multiple locations. Our storage igloos are monitored on a routine basis. Using near realtime monitors, and those two are the A cams and the minicams, or the automatic continuous air monitoring system, for the minicams. Our historical monitoring is done through the depot area monitoring system, which is stationary monitoring platforms around our depots that use tubes, and those tubes are collected at 12 hour intervals and analyzed. We also have a realtime analytical platform or an RTAP. It's basically A-cams or minicams in an RV that pulls up to the igloos or our storage sites, or if there is an incident, they show up and they perform realtime monitoring of either areas,

workers or igloos.

Next slide please. These are pictures of our A-cams and minicams. They run with three, five or ten minute cycles. During the operation of the plant, they run all of the time. If they alarm, people take action. If you are in a -- if they alarm in an admin area, everyone masks. After we mask, then people -- the visitors leave, then our workers come in and investigate as to what happened. They also have false alarms. We backed -- our false alarms are backed up with DAAMS, which is the next slide. These are historical monitors. It's a bank of 16 -- excuse me, eight sorbent tubes that are analyzed GCMS in a lab. If the minicams goes off, they take the DAAMS tubes that are running at the time and analyze those to confirm the presence of agent. With your near realtime monitors, there's no way to confirm. We use the DAAMS tubes as our confirmation.

Next slide. If there's an accident or incident, or we're doing entry monitoring for our igloos, we drive up to it with our lab on wheels, RTAP, and we hook sample lines that are prelocated within the igloo at the door, mid igloo, and at the rear, and look and see if they're -- before anyone goes in, look to see if there are agent readings present. If there are, then we come back in appropriate levels of dress and do leaker

isolation and try to find out which round inside of an igloo is leaking. They do that by breaking down by stacks and pallets. It takes a couple of days generally because you're analyzing -- you're covering, analyzing, and further breaking it down.

Next slide please. Our risk management approach, we verify our monitors on a daily basis. We use dilute agent to challenge them at the distal ends of the monitoring line, and then we correct that, we know what we inject, we look and make sure we can read that. And we have them located throughout our plants, as well as the mobile ones that go to our storage areas.

Our DAAMS methods are verified daily, both at the depot and at our demil plants. The monitoring of our process is complex. Across the board, hundreds of near realtime monitors that must be kept up with, and we monitor everywhere we can in the plant. We monitor our emission stacks, we monitor our filter beds, we monitor corridors where people are routinely going. We don't monitor the areas where we know there is agent going to be present, because it pegs out the meters. But lots and lots of monitoring. And then each time the alarm goes off, it causes a ripple effect through the plant. You have to figure out why it went off? Was it a false positive? If it was agent, who was there? Then those

people get automatically referred to the medical clinic for postexposure follow-up.

Next slide. In summary, we have a comprehensive occupational health program in place at each site, both on the storage side, which is -- I should have mentioned this in the beginning. Our storage mission is supported by MEDCOM. We have MEDCOM clinics. Our demil mission is contractors, but we all work together to have a comprehensive occupational health program for both agent and nonagent hazards. We do routine workplace monitoring and risk of exposure to determine the content and frequency of medical exams. Again, if you are potentially exposed, you go and are medically evaluated before you return to work. Each site has specific occupational health programs based on common programmatic items, which I am responsible for at the headquarters level. And we follow both DA and OSHA regulations. And our permits for our -- our stack permits are run by our state and follow the Clean Air Act. It's a very complex program and I can't do justice for all of the subject matter experts we have in our program, trying to give you a brief overview.

Our question that we are asking, I understand it is going to be assigned to a subcommittee. I think that subcommittee, they could understand our process

better if at some point in the next several months if they came to our chemical demil training facility at Edgewood and saw all of machine -- we have a mock-up full scale mock-up of our plants so that we can train or workers before they go into agent environments. They get training on how to put on and wear our OSHA level A suit. We have all of the equipment that they are going to work on present so that they can understand, when I go to change the strainer sock that is in the agent feed line for the liquid incinerator, what the lock is and how it works, so that the first time I do it is not with agent, it's in a training environment, people are there guiding them so they know what they are doing before they actually work with agent. It's a full scale facility. It does not have an incinerator. It does have a control room. It has all the process machines that we use to demil the nation's stockpile of nerve and blister agents.

Again, at the subcommittee's convenience, we can host a meeting for them and meet with our air monitoring experts, our physician, Dr. Bell. He would be here, but he is in class, long term. He will be done in a couple of weeks, as well as all of the operational experts. We have a very large staff that do this. And a lot of people have been doing it for a lot longer than I have, but it is a very, again, worker safety and

protection of the public health is the cornerstone of our mission.

DR. POLAND: Thank you, Mr. Cushen.

(Applause.)

DR. POLAND: I'm trying to keep us on time here. If there are one or two pressing questions. Dr. Lednar.

DR. LEDNAR: Wade Lednar. Some of the questions that were raised earlier about the acute symptoms of cholinesterase exposure, wondering if your medical surveillance data might be helpful. As you do your medical surveillance, and especially if in the workplace there is a worker who reports to your medical clinics reported acute symptoms, I assume that you would have some kind of an industrial hygiene confirmation about what was the exposure level of that worker that was associated in time with that clinical complaint. As you look at that data over time, is there any reason to think that the exposure levels are dropping, and our point of detection of onset clinical symptoms is now lower than we ever thought it was in the past.

Is there any data of yours that suggest we need to recalibrate our exposure health effect?

MR. CUSHEN: This is Dr. McIntosh. He's our contract medical director. We can do that, and we do look

at, from a programmatic standpoint, what were they exposed to. As far as the clinical or reshifting the baselines. We just did that with the CDC programmatically by lower the STEL, and worker protection rate. I don't think I quite addressed.

DR. MCINTOSH: I'll take a crack at it here. Thanks for the question, Wade. Over the last 25 years, I think we have seen a dramatic drop in the number of acute clinical exposures and also we've really got our arms around the monitoring technology. Back in 1976 when we first started this program in Rocky Mount Arsenal, we had over 150 cholinesterase exposures of 25 percent or greater. In the storage program today in the demil program, we've had one acute cholinesterase exposure in the last 15 years at our storage disposal sites.

We do many types of potential exposure evaluations. There are many circumstances, as Alan pointed out, when someone tears their suit or breaks the seal on their mask and they are in an agent environment, we will routinely medically evaluate them, to include an inventory of acute clinical health effects, cholinesterase levels, and we've never seen any clinical or subclinical evidence of exposure in any of those potential exposure evaluations that we've done since Johnston Allen in 1990.

We now have a second tier of more sophisticated biomarkers that we are using in any circumstances where we see a greater than ten percent depression in acute cholinesterase activity. We'll then do urinary metabolites for either isopropyl methyl phosphonic acid in the case of GB, or ethyl methyl phosphonic acid in the case of VX. So we have a secondary way of saying, yes we have a cholinesterase depression and yes, it's due to GB, VX, or some other organal phosphate. So I think we've improved that medical evaluation monitoring capability immensely in the last ten years

DR. POLAND: Okay, Dr. Shamoo.

DR. SHAMOO: Adil Shamoo. Having human subjects for patients in high risk environment to me is very valuable in terms of studying them if they are already in those environments out of their occupation. Regardless whether there is an association with the brain tumor issue we are discussing, wouldn't it be very reasonable to have an overlay of research protocol to do retrospective and prospective study; I realize the numbers might not give you statistical significance in all the subcategories, but nevertheless, they may give you trends and those would be very valuable as far as I am concerned.

DR. MCINTOSH: I think that's a very good point. In fact, we looked at doing a retrospective cohort study at one of the longest operating plants, which was Camdess, an R&D plant that was put in operation in 1979. and this was when we were concerned about -- particularly with mustard exposure, its long-term carcinogenic effects. We did a power calculation looking at the numbers of employees and the number of person years, and we found to our dismay, maybe not to your surprise, that the power they'd be able to see a relative risk of less than, say six to one, was -- you couldn't do it. So we would have to do a multiple site study to get enough person years, I think, to be able to see anything like Dr. Bullman saw. That is the power of your study with that large cohort. You were able to see a relative risk of less than two, and I didn't think that could do that at one site. We would have to do very broad studies to have significant power to see those sorts of subtle things.

DR. POLAND: Okay, any other questions? Dr. Oxman.

DR. OXMAN: The medical -- excuse me. Mike Oxman, San Diego. The medical records that you're talking about which include both military and civilian personnel, are those integrated into one system? Are

they electronic? Are they available, for instance, for this kind of surveillance, across all of your plants, all of your facilities?

DR. MCINTOSH: That is -- the answer is, there are a variety of different systems. Our civilian employee health records, which are military records, and those are retired in one location. The contractor medical records are mostly hard copy. We have one site that's transitioned to electric medical records using Occupational Health Manager, which is a software, commercial software. But that is not easily gotten at. That is one of the Achilles heels of doing that sort of a study.

DR. POLAND: Okay, thank you very much. We will move on. Our next presenter is Ms. Dee Morris. She will give us some background on using exposure standards to determine "How Clean Is Safe". Her slides follow the previous slides.

MS. MORRIS: Mostly what we have been concentrating on here is airborne exposure limits to determine whether or not an individual has received a dose of chemical agent. However, we use those airborne exposure limits to determine in decontamination when we are done.

Next slide. Why would we want to go ahead

and have decontamination standards. This is sort of intuitive, but obviously if you've managed to get a critical facility contaminated and you need to get back into it quickly, you are going to want to decontaminate it. You also have to return a facility to public use, and the standards that one might use for those two different types could be different. And then finally, and there wouldn't be a presentation by a lawyer without this, you have got to deal with liable.

Next slide please. When you are looking at setting your decontamination standards, you've got a number of things you have to consider. The first is the criticality of the space being decontaminated, whether or not you plan to occupy it with or without protective equipment. The material or the surface being decontaminated. Basically what you are looking at here is whether or not you're going to keep or trash. Because in some cases you're dealing with substances that are cheaper to replace than they are to decontaminated. The length of the expected occupancy. If this is going to be someplace that you're cleaning up and you plan on people occupying from here on out, you would have a different standard than if you were only having people go in for short periods of time. This would be the difference between the STEL the worker limit, or the general

population limit, depending on who and how long it would be occupied. Again, it is important as to whether you're dealing with workers or the general public, because as you saw in the previous presentation, there are different limits or airborne exposure limits for workers and the general population, because workers are being monitored and the general population is not.

You also have to look at whether or not you've got particular occupants, or potential occupants of the facility that are sensitive in any way. When I was working arms control inspections, we would take cholinesterase baselines for all of our arms control inspectors so that we would have something to work from in the event that we were exposed. And we had one particular individual that we sent in and his cholinesterase level at baseline was so low, that we could not allow him to be an inspector. So those are the types of things that you have to take into account.

Finally, and this is probably the most important one is the public perception. When we were cleaning up the various facilities after the anthrax letters, the public perception was what was primarily driving the efforts behind the decontamination of those facilities especially at the Brentwood Post Office, because the workers there were not accepting of the,

"We've cleaned it up. Just trust us." They wanted to make sure that it was cleaner than clean. And you're going to run into that with the public perception, especially if you are trying to return a facility, and I'm talking about not necessarily demil facilities or storage facilities. I am talking about facilities that might have been either accidentally or intentionally contaminated by any number of agents.

Next slide please. We do have some existing standards and the CBRN Contamination Hazards and Risk Working Group is actually looking at decontamination standards for all three types of agent. And the thing to note here is that you're dealing with fairly low numbers and that the standards are set by different organizations. And so there is no real consistency between them. And in some cases such as the chemical, I have listed the GPL for VX there. That is a very low number. And it's agent dependent.

Next slide. Well, what are we going to do about this? Well, first off, we have to answer the worker or the general population limit question, because it will determine whether or not we clean to certain levels. If we are talking about people who actually work in those facilities, perhaps some sort of surveillance could be started on them and we could use the higher

worker protection limit. If you happen to notice on the previous slide, the biological decontamination standard is zero viable organisms. And that's at a ten log kill. Many people believe that that is unnecessarily strict. And so we have to look at -- and it may be agent dependent, but we have to look at determining a realistic biological decontamination standard. As I mentioned earlier, there are some things that are cheaper to get rid of than to decontaminate. And this would always have to be something that would be weighed in any particular decontamination effort. The facility would have to be absolutely one of a kind, very very critical, must occupy before you would just automatically say, we are going to decontaminate it. Otherwise you would have to go through pretty much item by item as to whether it was going to be kept or decontaminated.

Finally, it is in fact possible to build a decontaminable structure. You can do that with epoxy paints. You can limit your flooring choices, and you can also limit the type of choices you use for surfaces on furniture. And so these types of things would be something that would be taken into account in determining whether we want to -- a high risk facility could in fact be decontaminable, and therefore, able much easier to be returned to final service. And that concludes my

briefing. Are there any questions?

(Applause.)

DR. POLAND: Thank you, Ms. Morris. Dr. Lednar.

DR. LEDNAR: Wade Lednar. I have another way ahead kind of question, but it may not be so way ahead. For those installations that have been on the BRAC consideration list, it's a question of potential future use of DoD either buildings, facilities, installations, whether or not that whole process for future use includes some restrictions about what would be allowed for future use; because there have been some experiences in some corporations where facilities have been decommissioned, property sold, future and different use put in place. In fact, put things like daycare centers into operations, and then questions come up about child health, and then the question runs back to who was the previous owner, and what is the possible connection environmentally. So I'm wondering if your thought process is going to include the structural considerations of future use.

MS. MORRIS: Well, obviously that affects the standard to which one would decontaminated a facility. And it is particularly important because several of the chemical demilitarization facilities are in fact -- their bases are in fact scheduled to be BRAC'd. That is an EPA

concern, and it is something that is in fact considered whenever a facility is closed. It's the ultimate use.

DR. POLAND: Dr. Lemasters.

DR. LEMASTERS: More specifically, how many DoD facilities are superfund sites? What is being done to these superfund sites?

MS. MORRIS: I can't give you a number on superfund sites.

DR. LEMASTERS: Approximately?

MS. MORRIS: I wouldn't even want to speculate.

DR. LEMASTERS: Do you know if anything is being done to the ones that are superfund sites, does anybody know, to eliminate them or to clean them up?

MS. MORRIS: That is something that the DoD is working on, and it is part of the closing costs whenever a base is closed.

DR. LEMASTERS: How about those that aren't closed?

MS. MORRIS: Well, there are some places that are more hazardous than others.

DR. LEMASTERS: Is Fort Bragg a superfund site?

MS. MORRIS: I don't know.

COL GIBSON: This is COL Gibson. The history

of Kelly and some of the other sites that you are aware of, the amount of effort that's went into cleaning them up before they close should be testimony to DoD's efforts in that area.

DR. POLAND: Ms. Embrey.

MS. EMBREY: I want to thank you, Dee, for answering those questions so adeptly. Dee works for me in the Chem/bio/radiological and nuclear and high yield explosive arena, so she really isn't looking at how we are dealing with the other kinds of things on a regular basis. She's not avoiding you because she knows, she really doesn't know.

DR. POLAND: Okay, any other questions. If not, thank you very much.

(Applause.)

DR. POLAND This issue in question to the Board will be taken up by the Occupational Environmental Medicine Subcommittee chaired by Dr. Lednar. You have the disk with the literature review. We'll also get you the GAO report that was referred to so the subcommittee can deliberate on those three questions that were asked?

COL GIBSON: I have a limited number of the hard copies of the Institute of Medicine Report that are available on the CD. I always have limited number of hard cover copies if anyone wants those.

DR. POLAND: Okay, we are going to shift gears now to infectious disease matters instead of the lesser issues.

(Laughter.)

As we all know, Pandemic Influenza is a hot topic. At our last meeting, LTC Wayne Hachey provided us with a briefing on Avian Influenza and Pandemic Influenza, and is here today to give us an update. His slides are under Tab 3.

LTC HACHEY: Next slide. And as you just mentioned, this presentation, although titled, "What's New With Flu" is an update to the presentation that was given to the Board previously.

Next slide. It's with a heavy heart that I have to say it, but the spread to Europe has resulted to the early demise of an icon.

Next slide. The agenda for my presentation will be an update of the current disease status, status of DoD readiness, to include antivirals, vaccine, plans, and communication. And then finally a request for the AFEB review of AI planning.

Next slide. But is there Pandemic?

Next slide. Only if you're a bird. And for those of you who are into birding, this is an endangered Hawaiian Stiltcheck who actually is about this tall, but

whenever they see people they get about this tall.

Next slide. Avian disease now is in 15 counties, with a recent spread to European Russia, found in ducks, chickens, geese, and a sum total of nine pigs who did not have clinical disease, but were seropositive. Other areas and species that been affected, swans in Croatia, appropriately turkeys in Turkey. In Romania, laying hens and ducks in a single back yard that then expanded to the local community. And then in Great Britain there were possibly two parrots imported from Surinam and housed in a quarantine facility, who might have been exposed to other birds from Taiwan.

Next slide. This chart depicts the spread of disease from July through October. You can see that South East Asia looks like it is has new disease, but actually that is just a disease that quieted down and then sprung up again. Then as time went on, you can see it spreading toward Europe. Most of this spread was thought to be due to either illegal or just commercial bird trade. And most of this, up and through Kazakhstan was probably the case. This recent leap to Europe though, it does appear to be associated with wild bird migrations.

Next slide. This is the same map, but instead of looking at the disease progression over time,

the red dots are domestic poultry and the green wild birds. Again, you can see that domestic poultry probably is the culprit up and through Kazakhstan. And then that last leap more due to wild bird migration.

Next slide. So we still don't quite know whether it is the individual at the top of the screen with either legal or illegal bird trade, or whether it's migratory bird patterns.

Next slide. H5N1 probably mutated to a highly pathogenic form in domestic poultry and then moved back into the wild bird population. And this represents a rather unique characteristic of the current bird flu. Most of the time it leaps to domestic fowl, kills them all off and that's it. This one is rather unusual in that it leaps back and forth between domestic fowl and wild bird population. And then tends to single out different members of the wild bird species. For example in Russia it was particular nasty to swans but didn't really mind geese at all, or it should say ducks, and then as it moved along, it left swans alone and was wiping out the duck population.

So again, spread may be primarily due to poultry and primarily fighting cocks traffic across borders with the wild bird migration again contributing to the spread to Europe. And if we're going to blame

anybody, it would be the Eurasian Tree Sparrow. But we really do need to have more knowledge about the ecology and epidemiology of Avian Influenza both in domestic birds and wild birds before it can really point the blame on one species as far as being the cause of the global spread or potential global spread.

Next slide. So much for birds. What we're really interested in is people. And despite a really high density of people and diseased fowl in South East Asia, here really had been a 136 total cases with 71 deaths since this all started. And although it really is unpleasant for that 136 people, considering the population density, this isn't really widespread disease yet. This year, there've been 92 cases with 39 deaths and still no confirmed human to human transmission. And all of the recent cases have been associated with intimate contact with diseased birds.

At the last Board meeting, we presented on problems with containment, and they've largely remained unchanged. The continued problems still point to where the birds are. And again, the red shows the density of poultry in South East Asia, and that is where we can see still our continued problems with containment.

Next slide. One of the main problems with containment is uncertain transparency. A case in point

is an H5N1 that's been circulating in China for at least a decade. However, it's not been reported because the information regarding epidemics of high path AI, have been considered state secrets until 2003. Currently there is only one laboratory in China that has permission to conduct AI research. So one thing we used to tell the residents in acute care, never look for what you don't want to find. This may be the case here. One Hong Kong virologist was quoted as saying, "Avian flu virus can be detected in most poultry markets in China."

Next slide. In fact H5N1 in China existed long before the outbreak in Hong Kong in 1997. If we look at the Peoples Republic of China veterinary journals, they suggested that H5N1 was widespread in China as far back as 1997. However in January of 2004, this was the first time the Ministry of Agriculture admitted that China had any bird flu at all. In the same year, China established an information reporting system for large scale animal outbreaks. And shortly after that, 49 locations across their county reported AI.

The good news is that China has become much more transparent recently. But unfortunately, their Ministries of Health and Agriculture have a history of continued poor cooperation and communication between each other.

Next slide. Well, we're not immune. There is still substantial poultry risk here in United States. California is one of the few states that actually licenses game cocks and there are three million of them in that state alone. We produce about 9.3 billion commercial chickens, and more concerning is a hundred million chickens in unregulated live bird markets here in the U.S. Now shifting from one two-legged species to another. There are 60 million foreign visitors to the U.S. and we visit other counties totaling about 60 million U.S. visitors. There is also 400 million crossings in from Mexico. And with current air travel, a fomite in Viet Nam can be in Boise within two flights.

Next slide. That leaves us to response.

Next slide. In November of this year the Whitehouse released its National Pandemic Influenza strategy. And with that strategy -- next slide -- there are a number of statements, the first of which directly impacts DoD. That's the federal government will use all instruments of national power to irradicate influenza. With that, our planning activities have been very enmeshed with the national planning activities.

Next slide. As far as DoD activities, I will be presenting a brief description of current surveillance

activities, antivirals, vaccine, communication and plans.

Next slide. In regards to surveillance, we are currently developing a joint surveillance center, and this is led by COL Ken Cox, so I have blatantly stolen his words. The Joint Health Surveillance Center is going to be organizing existing and proposed DoD health surveillance capabilities to achieve a comprehensive and continuous and consistent military health surveillance system with in the Armed Forces. What this will be doing is essentially adding glue to take all of our surveillance activities and combining them into on cohesive unit. This will help standardized collection reporting and analysis information, will enhance DoD's global situational awareness, and it will support initial U.S. government integration of medical intelligence within AFMIC. The goal is for early implementation beginning the first part of 2006.

Next slide. In terms of antivirals, the Department of Defense has purchased some 24 million doses of Tamiflu and this will be prepositioned in the EUCOM area for use in CENTCOM, PACOM and CONUS. There are currently no pediatric formations, but pediatric compounding instructions should be due by the end of 2005. There is anecdotal and animal data that demonstrates both efficacy and effectiveness for

treatment of the current H5N1 stands. However resistance has gotten a great deal of press lately, and in fact about four percent of adults and up to 20 percent of pediatric population can develop resistant forms. And this is a problem as far as the amount of Tamiflu we might have to use at future dates. The good news is though, is that resistant mutation has resulted in viruses that are either incapable of subsequent infection, or have a markedly decrease infectivity. We've also requested an additional seven million doses through supplemental OMB requests this year.

Next slide. So that's what. The important question is when. As far as Tamiflu, again, we purchased 24 million capsules. Fifteen million are expected by December 15th, another five million by 28 February, and the remainder by mid 2006. A release policy has been completed and will going out for staffing within the next few days. We also plan to purchase Relenza. This will represent about ten percent of the total viral supply. Relenza being another one of the neuramindase inhibitors.

Next slide. We've also positioned ourself to purchase vaccine, and we're positioned to purchase some 2.7 million doses of an Avain Flu vaccine. the vaccine is based on a 2004 Vietnamese clade which is the same vaccine that HHS is stock piling. Unfortunately there

is no cross reactivity to the Indonesian clade so it's use during a pandemic is still to be seen. It may prove to be a good primer. With a lucky mutation, it may be good enough for a primer and a booster or none of the above. This will be available to use around spring of 2006. We've currently purchased about 1.6 million doses of this and the reason why the disconnect between the 1.6 and the 2.7 is that 1.6 is all the manufacturer could make this year. If they can increase their productivity, then we'll buy whatever they can make. And those doses are based on a 90 microgram dose requirement. So as more data comes in as far as adjuvant and another antigen sparing strategies, our yield might be actually much higher. This is currently being stored just in bulk and this will enable us to one, increase the shelf life, and two again, wait for these studies before it's actually package and used.

Next slide. Communication. At the national level, the federal government has established a website called pandemicflu.gov. That includes the national strategy, pandemic plans for all of the government agencies as well as a number of the states. It includes monitoring data, travel advisories and guidance. Health Affairs has also developed an Avian Flu website that's listed here that provides information for our

beneficiaries, and will be expanded to provide information for providers and commanders. And Health Affairs has also established a DoD Readiness Watch Board.

Next slide. The watch board will provide leadership at the comprehensive AI situational awareness. It includes the current disease status, countermeasure status to include the vaccine, antivirals, antibiotics, PPE, ventilators, and so on. And it also includes our current planning status, which would include the status the current planning guidance and reference to pertinent documents.

Next slide. This is what the home page of the watch board looks like. If we are interested in let's say surveillance and detection, -- next slide -- next slide -- you would get a screen that looks like this. If we were curious as to what the current human disease toll was -- next slide and next slide -- you would see a charge that resembles this which has a location of the number of people, or I should say the date reported, the possible source and then the totals as far as deaths and cases for this current week, as well as 2005 and 2004.

Next slide. If we are interested more in birds -- next slide -- we click here.

Next slide. And you can either get a

tabular chart like we just saw or a map that would correspond to both the human cases and animal cases.

Next slide. If we are interested in plans -- next slide and next slide -- this would get a listing of the current plans and their status, and then the individual could click on each plan and get a copy of that.

Next. So all of this does take money. And the President has requested some 7.1 billion dollars for a national Pandemic Influenza response. And this includes countermeasures, advance cell culture techniques, vaccine procurement, antivirals, defense development, domestic surveillance and response and international efforts.

Next slide. In the list of how the money is doled out, DoD would receive 130 million.

Next slide. And our request for that 130 million would include purchasing vaccine that is currently in production, improving worldwide Avian Influenza surveillance programs, obtaining more equipment, for example ventilators and PPE, establishing a central information management system, laboratory diagnostic equipment and military to military systems.

Next slide. So what is next?

Next slide. Short term tasks, first is

completion of the DoD Pandemic Influenza guidance and our goal is to have that guidance consistent with the HHS draft, and the currently being authored national plans. We are also developing clinical practice guidelines, delineating the PHEO's role and determining priority groups for vaccine and antiviral use. In addition to this, again the implementation of the surveillance center, completion of the CoCOM Pandemic Influenza plans and determining DoD's role in the National Pandemic Influenza Plan, which again, we are fully engaged with integration at DoD and each component of that plan.

Next slide and next slide. So a great deal of progress has been made, but really much remains to be completed. And there is an vital need for an external group of experts to advise the department on Pandemic Influenza. Just for an example, to review clinical practice guidelines, potential modeling and vaccine and antiviral prioritization.

In that light, a request was initiated in the latter part of November 2005 to form an external and independent AFEB Advisory Board to advise DoD on matters relating to Pandemic Influenza.

Last slide. Actually this is a family member. This is Eleanor.

(Applause.)

DR. POLAND: Thank you for helping us get caught up here. Any questions from members of the Board. Dr. Lednar.

DR. LEDNAR: You started out by reminding us this an infection of birds. And I was wondering, can you describe for us what kind of central surveillance we have. For example, out in the Aleutian Islands, thinking of what's in Asia, perhaps coming this way, and coming from Europe and given the spread across the Eural Mountains what kind of awareness do we have for possible introduction to the western hemisphere of this infection.

LTC HACHEY: Actually the department of Agriculture and the Department of Fish and Wildlife have been actively engaged in surveillance in Alaska looking at that particular migratory -- bird migration pattern. And I think to date they have swabbed the undercarriage of I think about 5,000 birds now. And their activities have actually been stepped up over the past six months. And thus far they've found no evidence. In talking to the bird people, they feel that it is not necessarily one bird who makes this migratory trek, but it's kind of a piecemeal pattern that generally follows the migratory routes. Their best guesstimate is that we shouldn't see Avian Flu here at least with the migratory bird patterns, for another two years.

DR. POLAND: Wayne, a couple of questions. One you mentioned, the 90 microgram dose, but in the clinical trials it was taking them two doses?

LTC HACHEY: That's right. It's a 90 microgram dose, but two courses of that, 90 micrograms.

DR. POLAND: And then at least in some animal and in vitro studies, the antiviral, the amount of Tamiflu required has been almost double the usual dose for as long as eight weeks, and at least in those that have been treated to date, about half have died nonetheless, probably because they came late and got the usual doses. So is the amount that is being planned for purchase based on standard doses and length of time on some other model?

LTC HACHEY: The amount is currently based on standard dosing. Most of the folks who are coming into medical treatment facilities in South East Asia are coming in very late in the course. So they are clearly not following the package insert. There are a few though that have presented early and that's been primarily family members who were hospitalized and subsequently died from H5N1. They developed symptoms and reported quickly. And when they have been treated with Tamiflu, they responded nicely. So it looks like the ends are exceeding the titer though and the controls are just good awful bad, but it looks like Tamiflu provided early in

the course is effective. The animal data from what I understand is primarily in mice. And my understanding is that the comparability is low - there are researchers looking at different animal models, particularly ferrets to see if, one the efficacy is the same, and whether we do need to expand the dosage recommendations. But the cases in South East Asia have been using the standard dosing and again, when used early, those folks represented the survivors.

DR. POLAND: The other comment I might make is that to my knowledge, all the Tamiflu resistant viruses have still Senamivere (phonetic) susceptible. Dr. Kaplan.

DR. KAPLAN: I was just trying to recall the map. I didn't see any evidence of birds migrating into the Middle East. Do you have any?

LTC HACHEY: Not yet.

DR. KAPLAN: There is --

LTC HACHNEY: No disease yet. There is a report of H5N1 in I believe it was to Kuwait, and that proved to be erroneous.

DR. POLAND: Dr. Oxman.

DR. OXMAN: Mike Oxman. Is there any evidence at all that the therapeutic use of Tamiflu will have any effect on the spread of the epidemiology of the

Pandemic Flu?

LTC HACHEY: There is some modeling that suggests if you have early recognized outbreak that is fairly well defined in a rural area, that applying a lot of antivirals in that area can either stop the pandemic or at least limit it. But there are a lot, a lot of ifs with that. One, if it happens in the middle of Bangkok, it's probably not going to work. Some problems with the disease in fairly isolated or rural areas, those are the areas we have the least robust epidemiology. So the chances of recognizing disease in an area like that early in the course is at best somewhat guarded.

DR. OXMAN: One second question, a little bit related. The anecdotal evidence suggests that Tamiflu is effective in treatment to prevent severe disease. That is based on the assumption of 50 percent mortality if they weren't treated, but do we have any denominator data for cases that are recognized early in terms of what their outcome would be when treated?

LTC HACHEY: No. And that is one problem. We don't have good denominator data as far as the folks that we know have disease. Where it's probably more lacking is we don't know how many folks have been exposed to the disease had a mild course and are now going on their merry way or if there are any people like that at

all, whether it causes just severe disease or if it has the full spectrum like the 1918 flu where some folks were just mildly inconvenienced and other folks had a fairly significant disease and mortality.

DR. POLAND: Dr. Parkinson, then Shamoo and then Silva.

DR. PARKINSON: Mike Parkinson. Something I guess I either didn't appreciate or underappreciated was the growing awareness that H5N1 was in China as long as seven or eight years ago, and between their lack of infrastructure and their political will not to let anything out, does that change our characterization of this epidemic or potential epidemic? Does it give us more reassurance or less reassurance that we are seven to eight years into something that basically could have affected -- and this is a quarter of the world's population. It's not a small area. And also, so does it give us more reassurance that maybe this thing has peeked as opposed to something that cropped up three to five years ago vice the normal sero epidemiology, what happens with flu virus.

And the second thing is, given that it is that prevalent or may have been that prevalent seven, eight years ago, are we systematically going into China in any way to do sero surveys and to get a better feel

here? What if anything could we do to do that. Because it seems like it could be a potential treasure trove that I just never thought about. If it's all being discovered, please tell me. Because it seems like -- I was not aware of the wide prevalence as much as seven years ago.

LTC HACHEY: From what I understand, China is still somewhat of a black box, that there not terribly open to having folks zipping around the country doing seroprevalence rates. Their own laboratory infrastructure would suggested that they're not heavily invested in doing that either. I guess the first part of your question, I guess that's the good news/bad news, and to have a coin, which one is better. The problem is that it does mutate and it does mutate in China. At least some of the past concerns about transparency would make one a little nervous as far as the pandemic blossoming there before we could possibly contain it.

Again, on the bright side, the disease has been around for a while, probably has been infecting people there for a while and nothing terribly bad has happened yet. So I guess it depends if you're a glass half full kind of a person or half empty.

DR. SHAMOO: Adil Shamoo. I think most scientists agree that epidemic would occur, whether it's

in one year or a hundred years, we don't know. That is the unknown fact. However whatever governmental compliance processes are in place would greatly depend on morality and justice of those procedures and their continued communication to the public at large. What has at the national level or at the DoD level taken steps to ensure that kind of morality and justice is continuously thought about and communicated to the public at large?

LTC HACHEY: I can speak a bit to the DoD level. Again, the Department of Health Affairs has a, for example, a website for our beneficiaries that provides information about Avian Influenza antiviral use, who will be receiving antivirals and why. And as we have more information then that is added to our website. So that information is available. There are other DoD agencies that also have similar websites that is available to beneficiaries. An example is the Military Vaccine Agency has a rather robust website that covers Avian Influenza in additional to seasonal flu and a host of other communicable disease.

DR. POLAND: I want to make another comment on that. I was one of the contracted reviewers for the DHHS plan, and in there they -- which is now available. In there they comment on a public engagement process that they're undergoing. And CDC and other groups have

actually invited in groups of ethicists to look particularly at the vaccine and the antiviral. There are -- I forgot what they called it now, tiers or priorities for who will get the vaccine or antiviral and who won't. So they've approached that, I think, with that in mind.

LTC HACHEY: In fact, HHS has had a number of focus groups of citizens. It's a nice swath across the country that essentially asked what they would do with prioritization, and how would they deal with the ethical problems as far as the limited resources --

DR. SHAMOO: I just don't think websites are sufficient.

DR. POLAND: Dr. Silva and then Dr. Halperin.

DR. SILVA: Thank you. That's a very nice review. At National Academy last week we heard that on a subcommittee meeting, that the birds in domestic farms in Modova and also Romania, those that were at homes, those that were in big pens, housed in, they had not seen any yet, but they are looking to find a contact with bugs. There's going to be well known diversity of those bugs as you imply, from China, Singapor, down Gabon. And maybe this thing has been in China a long time and either didn't reach a critical mass to get into the migrating bird population, or has taken on an entirely different twist. We may see some hypervirulence come out of the

genomic analysis. My question to you because I don't know the answer is that the standard influenza vaccines have what 80 micrograms or so of --

DR. POLAND: 45.

DR. PARKINSON: 45, and this is at 90. If we have to go up in dosage the storage pools kinds of vials, is it easy to get in there and calculate what is a dose or are they all packaged in 90 microgram vials?

LTC HACHEY: As far as I know right now there are no packages. That it is all being kept in bulk storage.

DR. PARKINSON: So it would be easy to break it down, then.

LTC HACHEY: And one of the reasons for the bulk storage besides extending the half life, is finding out are adjuvants going to work or are there antigen sparing strategies going to work. So we may be able to get by with much less than the 90 micrograms.

DR. POLAND: Dr. Halperin.

DR. HALPERIN: Could you clarify whether there's an active surveillance system for resistance either the virus, birds or humans, as it moves around or is this all kind of anecdotal as far as resistance.

LTC HACHEY: Their residence to Tamiflu? To my knowledge, the current cases in South East Asia, there

isn't an active surveillance for resistance, however, the genetic analysis of each of those strains has demonstrated that there has been no significant shift or drift.

DR. HALPERIN: And that laboratory analysis is part of active surveillance system, organized?

LTC HACHEY: Not really an active surveillance system. An example is when there is a case let's say in Indonesia, samples obtained. It's actually run by both CDC and NMRU II our overseas lab in Jakarta that sample, when available, either the WHO and/or the CDC would do a genetic analysis to see if this is a change, but as far as active surveillance I think folks are just catching as catch can.

DR. HALPERIN: If I could follow up, then as these difference countries are reporting the virus, is there in vitro testing of those viruses for resistance.

LTC HACHEY: Not that I am aware of.

MS. EMBREY: This is Ellen Embrey. I urge you all to look at the President's National Pandemic Strategy. One of the last pages of that strategy is a series of I think ten principles that have been identified by the state department and the U.S. government to engage countries all over the world to agree to follow those principles. One of them are

surveillance and identifying and getting the sero types and sharing it with WHO, reporting on a regular basis and agreeing to work together to deal with strategic communication and emphasizing important public health strategies that apply since there is a scarcity of both antivirals and vaccines.

So I think it's important that in the context of what DoD is doing, we are doing what we need to do to protect ourselves, because we are also trying very hard to be part of the U.S. Federal Government as an international and domestic partner in preparedness for response both in this country as well as internationally. And so we had sort of -- we're schizophrenic, yes, we are. We are very much focused on doing what we can to protect our force to continue our mission. And we're also looking at what we may be asked to do to provide and support sustained global economic-- and minimize global economic impacts of a pandemic, both overseas and in the U.S.

So it's a very complicated thing and I'm not sure that we have all the answers yet. We haven't worked through with them all. There is a tabletop exercise being sponsored by the Whitehouse through the Homeland Security Counsel, the President's staff, I think the Vice President will attend along with all the principal

cabinet officials are going to go through an exercise and evaluate key questions about the role of the U.S. government in preparing both not only United States and working with the state, but also how we're going to work internationally to try to contain and minimize the spread of it once it is identified. I can't think that we have all the answers yet until we play a game -- a meaningful game and really confront ourselves with some of the hard issues. And we're not quite there yet.

DR. POLAND: Okay. Thank you, LTC Hachey.

(Applause.)

DR. POLAND: Our next speaker is Dr. Martin Tepper, Chief of the Communicable Disease Control Program for Canada's Department of National Defense. He's going to present to us some information regarding Canada's TB testing.

CDR CARPENTER: I'm not the speaker. I'll be introducing him. I just wanted to say Ms. Embrey, Dr. Poland and Col Gibson, fellow colleagues, thank you. I appreciate very much that you have given the small but hard hitting Canadian contingent some time to speak. It's my pleasure to introduce Dr. Martin Tepper who has join -- actually he worked as a family physician, joined the Armed Forces in 1975, did postgraduate training in community medicine which included two years in Kentucky

as an epidemic intelligence officer, where he was made an honorary Kentucky colonel. Following that, he served ten years in the Canadian Forces, mainly in the Surgeon General's Office looking after, among things, global disease control, occupational health, health promotion at various times, and of course, fixing coffee for the Surgeon General.

In 1902 -- sorry -- In 1995 he retired as a military physician, only to work for Health Canada, which is basically Canada's public health service. But a few years later he saw the light and returned to work as a civilian for the Department of Defense. He is now Chief Medical Advisor in Communicable Disease Control Program of Force Health Protection. Dr. Tepper is well known and well loved and respected by all in the Canadian Forces.

(Applause.)

DR. TEPPER: Thank you, Commander. The Commander and I go back some time. I used to be his boss. When I came back here as a civilian he was my boss. So here we are. It is a pleasure to be here and to presented to you. I doubt that I am going to give you any kind of real new insights, but we will go through kind of what our thinking has been about tuberculin skin testing. I am here at -- I was actually David who sort of brought this forward and encouraged me to come down

and talk to you and he was also, when he was my boss partly responsible as a supervisor with the decision making around the use of tuberculin testing, so if we have gone off track here, he's to blame, okay. Not me.

Although I am listed as the Chief Medical Advisor, in fact I am the only medical advisor, and I'm not actually -- I'm not the head of the Communicable Disease Control Program who is a military member.

If I could have the next slide please.

Canada and United States, we're different. Some of us talk the same language. Some of us don't. To compare the two, our land masses are probably about the same, although I didn't mention that there. Our population, the ratio of our population, United States to Canada is about 9.2 to 1, which would be the benchmark that one might use for subsequent roles. Our regular force is considerably smaller proportionately than yours. Our health services are considerably smaller than yours. I can only get on the web the number of health care workers uniformed regular force in the U.S. Army. We have three positions for communicable disease control physicians when they are filled. Currently they are all filled. As of about a week from now, only two of them will be filled. Whereas you all have probably a whole bunch, and a whole bunch more than us.

When it comes to tuberculosis we are about the same. Those numbers, if they are a surprise to you in terms of the numbers, are the estimate from the WHO in terms of sputum positives, the rate sputum positives per hundred thousand, out of a WHO report.

Next slide please. Canadian Forces has for a long time used tuberculin skin testing as have all other military forces -- western military forces, including yourselves. We've tested before and after deployments with a suitable time -- waiting suitable time after return from deployment before we test. We have done for the last 15 years or so, we have routinely done two step testing when it's applicable. We test recruits although it's not in the slide. We used to test recruits on entry, just as yourselves do. We use five tuberculin units intradermally and it's read in the standard fashion, using induration. Our cutoff for a significant reaction is ten millimeters or more than or equal to six millimeters if the previous one was five to nine millimeters. We estimated that we did probably, if everybody followed the rules and had the tests like they were supposed to, then we'd do about 20,000 plus TSTs a year, if the policy was closely followed, and that would take up about 555 person days needed, which is a loss of about two or so persons from a very small pool of people

to start with.

Next slide please. Here is some data that was reported. A lot of it reported passively before we changed our policy in May of '04. We had very little disease reported to us. In the ten years prior to this slide, which was data up to early 2004, we had only had two known cases of active tuberculosis in the Canadian Forces. One couldn't find any information on in terms of where the source case may have been. The other one was a primary disease that occurred several weeks to a couple of months after an individual had been deployed to Bosnia. A very small number over a ten-year period. Among the TST positives, as I said, we did recruits on a routine basis, and we had over the period August '02 to August '03, 36 TST positives for a rate of almost one percent among our recruits. Now that is pretty good data we had. We are fairly sure that we had complete reporting on that group.

Getting to groups that we don't have such good reporting on, we had -- because we used to do pre and post deployment, from 2001 to 2002 predeployment, we had at least seven PPD positives, all converters because we had done testing, of course, before either recruit, or they have been deployed before and had been tested.

Postdeployment, all of whom should have had a

predeployment test, although I can't guarantee that that actually happened, I have some examples. An early rotation that went to Afghanastan for six months, was mainly Army, came back and there were six converters in that group for a rate of 1.3 percent. The millimeter size of those TSTs was on the low side with that, a mean and median of 13.5.

Of particular certain was that we had three warships go to the Arabian Sea as part of the antiterror effort. And they went for six months. They touched land eight times for like about a day each time, and there was in the fullness of time, no case of active tuberculosis was found on any of these three ships. And we had 16 converters among those ships. These are small ships. These are 250, 300 people a piece. That was of concern. Again, no source case known, no exposure to the local population, everybody -- I always bring up, well, you know, if you had a prostitute contact in an endemic area, you know, this might give you tuberculosis. Well, it might give you a lot of things, but it probably won't give you tuberculosis. Then among all deployments, again from 2000 to October '03, we knew of 52 converters, of which the millimeter readings, mean median and range are there again on the low side.

Next slide please. We looked at our TST

positives, and basically they were all asymptomatic and they all had negative chest x-rays. In all of these, we never could find a source case. Whether it was a case in Canada predeployment, or a case postdeployment, we could never come up with a source case. Most of the millimeter readings were less than 15, or 15 or less. And it did raise to us the concern about false positives from the use of TST in a low prevalence population.

Of 149 reported TST converters from 2000 to October of '03, almost four years. These aren't all reports, only the ones that we had. A minority indicated they were actually going to use INH or that was recommended. We have no idea about the completion rate on those individuals. Further we did not have the information about why INH was not used. We used at that time 35 year cutoff in terms of use of INH or not. Most of these converters were in fact, allegedly recent converters, so in fact INH would have been well indicated.

While not on the slide, we did follow closely two rotations to Bosnia which would be about 800 people each, I think, or so. And the -- although we monitored them closely, we sent out notices to the medical people and we put command emphasis on it, for one rotation the completion for TST was 21 percent and for the other was

41 percent. Some of these problems may be familiar to you. So when we looked at it we had some concern that maybe we are doing more harm than good by use TST. So we reconsidered whether we should use -- How we should use TST in the Canadian Forces.

Next slide please. The assumptions that we worked on were that tuberculosis is usually hard to get. It is a quote from CDC, presumably a competent authority to make the statement. Other than for contacts of cases, newly acquired tuberculosis infection is hard to diagnose with confidence. The tuberculin skin test, as you know, has litany of problems. Proper application, subjective reading, imperfect sensitivity and specificity, and unfortunately you can't distinguish by in large between those who are truly infected and those that are not infected. And hence you wind up having to offer chemoprophylaxis to all when it's indicated. Further chemoprophylaxis for converters or newly acquired tuberculosis infection has problems related to compliance, side-effects and it is not -- I mean it's fairly good, 80 percent effective.

Next slide please. This slide which you already know from your own experience, it displays with prevalence of disease on the x axis and positive predictor value, a number needed to treat or to prophylax

to prevent one case of tuberculosis, and standard thing, if the specificity is 99 percent, probably what it is in TST if properly applied, the life time risk of tuberculosis disease of ten percent, that as the prevalence of disease goes down, the positive predictor value goes down, and as the prevalence of disease goes down, the number of people you need to treat to prevent one case goes up. We suspect that we may be -- in terms of your own conversions, somewhere in .5 to one percent. Looking at that we decided that we probably were giving a whole bunch of people prophylaxis who didn't need it. It was of no use to them personally, because in fact they weren't infected.

Next slide please. Why is the specificity of the tuberculin skin test not a hundred percent. The usual things. Cross reactivity with environmental nontuberculous microbacteria. Studies done in Quebec -- now Quebec isn't usually considered a high prevalence area for nontuberculous microbacteria but in this study in fact they found in Canadian borne high school students and young adults that the skin test positivity for intracellularity was one to two percent. So in fact nontuberculous microbacteria does obviously occurs in Canada and may be more frequent than we had thought

Prior BCG can cause -- can interfere with the

specificity of TST, and most province in Canada did not use BCG but the provinces of Quebec and Newfoundland did in fact do it until the early 1980s on a regular basis. Of course if you don't apply it properly to TST, and don't read it properly, you got both false positives and false negatives from doing it.

Next slide please. Does anybody care whether there is a false positive. Of course we care and for the reasons which are up there and they may be others. We were concerned that at least for the patient, the patient who has a false positive TST, although you can't tell them whether they do or they don't, has a problem, they are labeled as having a disease that may kill them or maybe transmitted to their love ones. They are taking a drug, which they would take a drug which has some harm associated with it, to no benefit in their own case. That is they are not infected. We would -- they would need to be medially monitored while on chemoprophylaxis and there is always the chance because we did, we would find a number of these predeployment, there wasn't a chance that in fact if we couldn't monitor them when they were deployed, that in fact they wouldn't deploy. They may have been good for them or not, I won't say. And lastly, we could not use the TST in the future then for contact assessment of an actual patient with

tuberculosis. Important too, why are false positive TSTs of importance to the organization, because it can raise unwarranted concerns regarding tuberculosis transmission amount specific units and specific deployments. In the early 1990s as I think David will remember. We had a particular group come back from Bosnia who had a number of TST converters among them. And no cases of tuberculosis and this issue was raised in the House of Commons to the Minister of Defense and got a lot of media play at that time. As it turns out, the investigation which I did not conduct and David didn't conduct either, the investigation decided that the problem was that we weren't using two-step testing at that time. Had we used two-step testing, this may not have occurred. Since that time, we used two-step testing much more frequently. And, of course, a false positive TST diverts resources. So are we doing more harm than good?

Next slide please. Because we also benchmark to what is happening in the civilian community, we looked at what the recommendations of others were in relationship to tuberculin skin testing and travel or in our case deployment. The Canadian tuberculosis standard says that if you are more than a month in a high prevalency area, you should considered pre and post tests -- pre and post travel tuberculosis skin testing. The

Canadian Committee to Advise on Tropical Medicine and Travel used three months as the cutoff.

Next slide please. Yourselves looked at the issue back in 2000 when it was brought forward by, I think it was the Air Force at the time, whether there could be risk base tuberculosis screening policies, raising as I understand, although I wasn't there and I don't have the transcripts of it, raising similar issues to which I have addressed, that we had concern about, as in the quote from the BG Murray up at the top. The AFEB's recommendation at the time was that -- well, you can read it. But said that, Gees, yeah, it may not be all that worthwhile and gees, you know, in some circumstances, you know, you may not be at an increased risk of getting tuberculosis, but we could -- we ourselves, when looking at this, couldn't understand really why the AFEB put in the last sentence. Went on to -- well, despite that, we still recommend that you do it. Okay. The next paragraph after this, which isn't on here, the AFEB did say if fact though, that if you can come up with an epidemiologic base risk assessment tool that in fact you might want to think about using it. There was none x stamped at that time and I don't think there's any x stamped at this time either.

Next slide please. Everybody seemed to

recommend the use of tuberculin skin testing for travelers or for deployment. There's at least one contrary review in the literature that one can find, and this is by Ryder who said, because of the problems with prophylaxis with determining risk, with false positivity, that he thought that in fact the most rational approach was to do nothing and wait until a case occurred. Have good surveillance for cases. A lot of people -- at least my superiors weren't all that enthused about doing that.

Next slide please. What is the risk of newly acquired tuberculosis infection from deployment and travel. Unfortunately there is only one reported prospective study of the issue, which indicated that if you go to a high endemicity country and you live among the locals and you drive in their buses and you stay in their homes and stuff, gees, you might actually over time, you might acquire the same tuberculosis rate as the local population has. And that makes some sense. The cutoff in this setting, they found that if you are going for three months or more, that the risk was elevated less than three months, it probably wasn't elevated. This study to us anyway, wasn't applicable to our -- most of our deployment.

There have before several retrospective studies done in response of a recognized outbreak. Some

of them done by the U.S. military. Some done on aircraft in the civilian sector, but those are retrospective and are based on, you know, actual cases that have occurred and people have looked back, of course.

Next slide please. Although the Canadian Forces is small, it does deploy to a lot of places. Now a lot of these places on the slide, we are only talking about a small number of people, a handfull to two hand full of people, but there are some where in fact the numbers are higher. In Afghanistan, for example, where we have about a thousand people now and will in the next few months have two thousand people. We do deploy and a lot of deployments are to TB endemic areas or particularly high risk areas for tuberculosis.

Next slide please. Why do we think that the risk from newly acquiring tuberculosis infection for our members on deployment is likely low? It's because we have little contact with the local population. Most of our contacts are of short duration, out doors, little close contact, little prolonged face-to-face contact. Most contacts do not have tuberculosis disease and Canadian Force members are well nourished and healthy. Now our deployments aren't necessarily like yours. We deploy only for six months. We tend not to be in battle by in large, at least in the recent past. So whether

this applies to yourselves or not, I don't know. It certainly seems to apply to us.

Next slide please. Here is an aerial view of Camp Julian which was the main Canadian camp in Kabel. There is not much integration into the local community. There is a big barbed wire fence around the whole camp, and the nearest person, Afghanistani that lives around there must be, you know, half a kilometer away or so. We tend to develop camps similar to this, perhaps yourselves do too, where in fact we don't integrate particularly with the local community.

Next slide please. On the left where there are patrols, mounted or unmounted, they are done outdoors, by in large. We do have some contact with the local population indoors as this major on the upper right that was talking to a local Afghani district governor I believe, about arrangements. And I just threw in the hockey slide. Probably your guys play football all of the time, right, no matter where they are. Even in the summer in Kandahar our guys will put on the uniforms and play hockey.

Next slide. Our conclusion, David's and mine, was that -- and the people we work with, that in fact we should change our tuberculin skin testing policy. And the policy that we came out with was that we wouldn't

do any more predeployment testing unless it was clinically indicated. And this to us would avoid the false positive problem because there's very little risk for our people in Canada for tuberculosis. We do routine postdeployment testing for all members if they have been in a high prevalence area for eight or more weeks, or if they provided direct care to the local population for any length of time, for example, health care worker.

If a person on postdeployment testing was positive and there was no clinical or radiologic evidence of disease, or in no known exposure, we would consider that individual as a recent converter and offer INH prophylaxis for nine months.

Lastly that we would institute a questionnaire for the recruits to try and tease out those who felt that they were members of first nations or foreign born who are the ones who are driving the tuberculosis endemicity problem in Canada. We carefully said that going to this policy seemed to be pretty good but there was no guarantee that we wouldn't miss an actual true converter who might actually go on and develop disease. We had a bit of a hard sell. Our decision makers, just as yours are appropriately conservative, but we ultimately did get a buy in. We did consider increasing the cutoff which is ten millimeters

in Canada to 15 or even 20 millimeters to make the test more specific although it would be less sensitive. But there's no Canadian data to drive that. We wouldn't know where the cutoff should be, and it would be contrary to the Canadian tuberculosis standard and everybody wanted to benchmark as best as we could to the civilian standard.

Next slide please. Here's some data after the change in policy in May of '04. We have had one case of tuberculosis reported to us, not related to service. A lady who's mother had developed active tuberculosis and transmitted to her daughter, had nothing to do with service. Among TST positives, we have a rate of TST positive among recruits who are either first nation or foreign born of 9.3 percent which of course would seem that obviously they did increase the prevalence of tuberculosis infection among that group by using the questionnaire.

Postdeployment for Afghanistan where we have data that we can rely on, the rates are 1.3 percent in Afghanistan and 1.3 percent in Balkans, and 2.1 percent for all deployments.

Next slide please. We did propose early on that we use a questionnaire to try and tease out the higher risk for acquiring tuberculosis while on

deployment and we used this questionnaire. Whether somebody was going to a lower risk area or higher risk area for tuberculosis, we had certain criteria that we would use. Unfortunately we still couldn't -- the surgeon general at the time, challenged us that this wasn't a validated questionnaire which was entirely true. We couldn't find a validated questionnaire, and if somebody has one, please let me know to try and tease this out. We actually only used the questionnaire one time and these are guys coming back from Afghanistan, and among those who were questionnaire positive, we had a converter rate of 1.7 percent. And among those who were questionnaired negative, we had a converter rate a 0.7 percent, a difference but not a statistically significant difference.

Next slide please. Could we validate a questionnaire or this questionnaire? Probably can't. There is no way to distinguish false positive TSTs from true positive. Progression disease is low and slow. We'd have to follow a whole lot of people for a whole lot of time to be able to validate the questionnaire. And lastly, those who are questionnaired negative yet false positives unfortunately, and the false positive rate may be similar to the true positive rate in the questionnaire positives, and so we'd never be able to sort it out as

far as we're concerned.

Next slide an this is the last slide for those who are really getting munchy hungry here.

Future possibilities that we will consider versus the use of the questionnaire which has face validity to us anyway, to guide the use of TST. The use of interferon gama assays which I believe the U.S. military uses and others, it's not available in Canada, not licensed in Canada, there is no PE cutoffs for it. It would seem to be a better test and maybe once it is established in Canada we may go to that. We need to bolster quality assurance for the placement and reading of TST. We have done some work in that, but it's of a relatively minor nature. And lastly, we'll toy with the idea, but probably won't be able to sell it, of not testing anyone postdeployment and just let -- and if the cases occur we will treat them and follow them up as appropriate, which may in fact be a legitimate thing to do. That would be harder to sell, even harder to sell, I expect. That is it. Thank you very much for your attention.

(Applause.)

DR. POLAND: The cafeteria stops serving at 1:00 so any burning questions.

Okay, COL Gibson, any administrative remarks.

COL GIBSON: Just that we'll be able to eat in the cafeteria, goes through these doors get in line, we'll eat over there and then come back here at 1:30.

DR. POLAND: If I could have Drs. Gray, Oxman, and Silva eat lunch with me.

(Lunch break at 12:35 p.m.)

(Afternoon session begins at 1:37 p.m.)

DR. POLAND: Okay, well press on here. COL Gibson, any administrative comments first?

COL GIBSON: Not at this time.

DR. POLAND: Good. We're going to launch right into Adenovirus vaccine. CPT Midboe was supposed to give the program update. He's ill and understand Dr. Allan Liss, is he here, will be substituting for him. So Dr. Liss the next 30 minutes and ten for discussion is yours.

DR. LISS: Very good. Thank you. First of all, it's a pleasure to be here and kind of a surprise. I was just really coming to listen and found out that MAJ Midboe was ill, hopefully not bad though. But I will try to give his presentation which I have seen in various forums. And I will try to give it as CPT Midboe will, obviously not being able to fill his shoes, but I know he has a particular message he wants to give. And if I feel the need to editorialize, I will add that. But I do know

that he feels his role as the project manager is to give a particular message on this Adeno project.

I think in summary, as you'll see, the message is that progress is being made, but according to being a good project manager, according to his original time line, we have some slippage moving out. And explaining, visualizing and by all means, exposing the slippage and the reasons for it I think is something that MAJ Midboe would want to see here, and I'll try to share that with you.

Next slide please. This is a general outline here we're going to be going through. I'm going to spend very little time and I would imagine MAJ Midboe would as well, on the clinical, as an excellent presentation from COL Sun is going to follow this. But certainly stop me if I fly through too fast on some of these.

Next slide please. As we all know this is something we have been working on and certainly as a representative of the sponsor Barr-Duramed this is a passion that we share with the military to work with restoring a very vital vaccine to the military, something I think we all share here.

Next please. Our objective, of course, is not simply to make something, but make something that is safe, effective and something that we are proud to give

to our military with the stamp of the FDA.

Next please. Again, in history, something that we've talked about at several of the other AFEB meetings that I've been with. It's a storied history. Starts with the contract being given to the Barr Laboratories and an organization called Vacgin and many of you may know Andy Tall who is the representative with us on this team. We built a building in our Lynchburg, Virginia facility that is dedicated solely to the tableting of the Adenovirus. This is a rather unique delivery form. It's an enteric coated double tablet with a core in the middle containing live adenovirus type 4 or type 7, a coat around it, an enteric coat so that this actually is a vehicle for delivery to the upper intestine of live adenovirus.

We've had a successful Phase 1 report, phase and clinical trial, and again COL Sun will present about that, and continue our critical efforts and we are now deep in concert and conversations with the FDA about that Phase 3 trial and allowing us to progress to the licensing event.

Next slide please. This is the project manager's best friend but everyone else's biggest enemy of our infamous GANT charts and as we plot this extremely complicated series of events, one of things that you can

notice, which I can't see, but there is about an eight month delta that we have. So we are moving up from our original plan which was based on some basic assumptions when the contract was first and today there is a slippage. And as we have talked about before, the basis assumptions of the original contract was that this was going to be a technical transfer of a product previously made by Wyeth, approved by the FDA, used in the military and shown effective, and then was going to be, Wal-lah, was given to the next manufacturer to make the recipe and have the cookies come out the same. Practically speaking, this has been far from a tech transfer. This has been a lot of development and a lot of getting today's machinery and today's manufacturing processes to work with the tablet in the past. This is something which the clinical trial experience has been helped by the FDA in many regards, and that they are helping us as if this were not a new product, but something that has a history to it. But of course, as you'll see, that doesn't mean that it is not going to have to prove that it is safe and effective in multiple populations. So we do have some current slippage that we are talking about.

Next slide please. This is just a little summary of the production parameters. We are talking about a performance characteristic of a tablet that

delivers the adenovirus to the upper intestine, something which we want to have a shelf life of approximately two years at refrigerated temperatures. These are things that were achieved by Wyeth at the end of their manufacturing history before they stopped making it. Took a lot of experience for them to extend it to two years. We have a facility that is being made -- that has been made for GMP vaccine development and material. It is critical to understand that we are very close to the manufacturing process that we are going to be taking to FDA for final approval. And why I say very close, is obviously the next step is integrating the manufacturing progress that we've made with the clinical progress that we hope to make in the very near future.

And just as a point to keep us remembering, all of this -- all of our successes will be dependent on being able to successfully make lot after lot after lot of our adenovirus. That is our current focus and our goal of our program as we speak.

Next slide please. This is a very brief summary and I'll just give you a very high level view because you'll hear a lot more detail from an expert, from COL Sun. We had a successful exposure to a group of military. It was not recruits, it was a group of trainees into the medic program, and this essentially was

our normal healthy human-being population to do essentially the first two units for this tablet. I think we heard the last time we met at least in Fort Detrick that it was successful and that it was well tolerated. We saw an immune response, certain version in the population, and I think that this is certainly a supportive trial for us to move forward to other clinical trials. This has been discussed with the FDA and their concurrences that it is not the slam dunk home run for lots of reasons, including small population size, but it is sufficient for us to feel that we can go further and forward to other additional trials.

Next slide please. We are trying to in our strategy, and so far it has been accepted by the FDA, is go from this first in human's trial to essentially what we -- our last trial, Phase 3. The design of this Phase 3 is far from simple. We have gone through this and you will hear some discussion I'm sure from COL Sun, with lots of discussion with the FDA. And just to kind of summarize what we have recently heard, as recent as last week, is that the FDA is interested in showing a couple major things. These certainly are things that we find quite acceptable.

One is they want to show that the vaccine is effective, so they're looking for an efficacy parameter.

This is obvious, something that they need to do. Slightly different from our original thought. Remember, our original though, if you look at the way the contract was originally proposed, since there was historical experience, it was thought that perhaps a serum conversion immune surrogate would work. I convinced the agency that this new vaccine in fact was the same as the old vaccine. The FDA semi-convinced of it, that's my phrase. They would like us to do efficacy trial and a parallel, actually look for seroconversion in the same population. This is now being sized by statisticians to be sure that when we do this trial, it actually gives us a weight from the data.

I think the most important part of the trial as far as simply logistics is the FDA is also interested in showing or be able to demonstrate that the more obvious adverse events are going to be either present or not, hopefully not. By that that also is going to increase the population size. So our original plans of having a small, essential bridge trial of a thousand people are not going to happen and we are now looking at the next variation. And I am sure that COL Sun can give you some insights for that. This is being planned as we speak, so this is an ongoing project that in the next very short few weeks will be the heart of the design of

the Phase 3 trial.

Next slide please. In parallel, of course, to the clinical aspects of it, is we want this to be a vaccine that is approved by the FDA, so we are also dealing with the various regulatory sides of this, that would eventually lead to a biological license application, a BLA for this vaccine. These are going quite well. Obviously what the FDA is interested in is a complete description of the manufacturing process, the good old CMC, chemistry manufacturing control section, and of course, waiting for the results of the -- actually how the vaccine performs in clinical use.

Next slide please. DoD has been supporting the project recently and this is appropriate time for them, so I don't mean recently as if they weren't doing their job. But they are adding a quality element to it, and the offices under the DoD have been gunned the audit systems of Barr Laboratories and Duramed. We find that that's very enjoyable. We produce many commercial products, so the FDA is in our house all of the time. So having another person giving us advice is something we appreciate, and we understand that certainly this is one aspect of any product that has not simply something that works, but it is something where quality is built into it, and that we can be proud of the project we're

distributing and certainly this one being put into our military, we're even more proud. We want the quality to be strong. So this is an ongoing process and I believe the DoD's audited our Lynchburg site. They are going to be looking at some of our computer systems and eventually will have the entire quality system of the manufacturing audited.

Next slide please. Now here's something which I definitely will try not to put my slant on it, but put on to DoD slant. Because for procurement, you know, as far as the sponsor side, we want to make it, and of course we want the DoD to sell it. From the DoD side this is I think a critical issue, and I believe I would be saying what MAJ Midboe would say, is that this is -- he's trying his best not only to allow this project to succeed to license, but to allow the actual end product, the vaccine to be purchased and purchased at a price that the government is willing to and able to afford. And this is an ongoing process. We have by our contract -- we really don't need to, and I'll -- this is a Barr comment, so put it in the record. We are trying to do the best we can to cooperate with MAJ Midboe, and it is really important that everyone understand that this is a cooperative event and we are not simply going to sit by and let things happen. We want the military and the

government to be able to afford and make this work. So this is going to be an interesting things that's going on in the near future, and certainly a nice focus for MAJ Midboe and I think he's doing a fine job in getting this approached.

Next slide please. Not to beat a dead horse, but unfortunately the disease is still out there. This is something that we need and the fine work that is going on by the military surveillance. I wish I could say that adeno has gone away. It's no longer a problem in the military, but it's not. It is a problem. And it's something that we definitely still do need and want to have protection. And this vaccine that has shown protection previously, there is ever reason in the world that we should get it back into our troops.

Next slide please. Certainly funding is an important effort. Perhaps what we look to MAJ Midboe the most and he does his best to make sure that the various things we do are funded. It should be highlighted that the interactions with the FDA and the guidance from the FDA to do a trial much larger and essentially much different than originally planned, is causing us to have a scope change. This scope change is going to affect obviously MAJ Midboe's budget, but it's something that we need to do to get the project licensed. It would be

great if our original plans, based on original assumptions had worked, but there's a lot of reasons those assumptions were invalid from the start. So now we are on a good path of clarity and this clarity is going to constitute or going to be driven by a scope change. And that scope change will be coming from Barr very soon.

Next slide please. So moving forward, we have a number of events happening, obviously manufacturing and our goal in manufacturing is to stockpile as much product as we can while we are making plans to go forward and do what needs to be done. Obviously you just don't stockpile vaccine at the stage that we're at. We are also developing stability programs. We are also developing additional methods of help us assess the potency and the viability of our vaccines and move forward. So a lot of work is going on in the manufacturing stage. The clinical stage again you'll hear from COL Sun, a lot of activity as well. The design of this large clinical trial, large in some respects, small in others, is certainly the number one focus to get this to the market place.

This is parallel, the regulatory group and clinical are working to make sure that everything is in line and all of the proper documents and procedures are followed. Quality from the DoD side is being again used

to make sure that by the time we are ready for license, the DoD will be have confidence of the -- compliance. This will prevalent of course to ultimate quality observer which is not on our end users, but it's FDA. They also will be monitoring the systems, probably end of next year, beginning of the following year.

Finally, last but not least, the funding, the cost increase, the scope changes, those things all have to fall in line and we have to be prepared and sure that everyone is comfortable with how we're moving forward. I think that's the last slide.

So the next three months, we're going to completing the validation master plan, actually the execution of it, producing additional vaccines and initiating the various clinical protocols.

Next please. We do have a number of risks as you do with any vaccine particularly biologic. This one I think is something that we don't think enough about. With the biologic you've got multiple steps. You're growing something from a living cell, a live virus, although it's pretty routine, but it is -- there are multiple steps in processing. As these steps -- anyone of these steps fails, we lose a lot. Our goal is again to stockpile. Currently we're at the beginning of that, so if we lose a lot, we lose time as well. We are hoping

that with all the stars in alignment and our fingers are crossed, that we can proceed with that.

We have lost a lot in the past. It was fortunate that at the time we had enough supply and enough lead time to do a clinical trial that it didn't kill us. So this is something we're always worried about is that ninth hour failure of a lot to perform or something else.

We are also looking at various aspects of integration of the trials with the population that we need to test. And obviously we know that the job of our trainees going into the military is not to be a part of a clinical trial. They've got lots of more important things to do, so it is great the cooperation we've been getting from our military colleagues to help coordinate the activities of the clinical trial with the normal -- as normal as possible, people can run with the epi training basis.

Obviously the cost issue is something that the DoD is going to be dealing with. And any of these issues, and all of these issues in combination, will have further impact on the project.

Next slide. Now it's the last one.

And of course the take home message is, right now it looks like we've lost eight months, and in

reality, we could gain some time back. There's possibilities of doing the trials in multiple sites and being lucky to save some time. On the converse, we could lose some time. So I want you to be aware that we have a goal now of -- moved out a little bit, but this is still until we really -- probably a year from now -- until we really have all the final pieces in place. It is the job of MAJ Midboe as the project manager on the DoD side and the job of myself as the project manager on the sponsor side, to push everyone involved, encourage them to hit not only this timeline, but try to save some of the time it looks like we may have lost. I think that is what MAJ Midboe would want to have said. And I'll be ready for any questions if you have any.

DR. POLAND: I do want to -- it's well known to most of our Board, but maybe not to some of the new people, that the Board has had a long sustained and continuing interest in this issue. In fact I would say it has probably been the one issue that the Board has been engaged in the most over these years. So I know it is well known to you, but this is a very, very important issue. We have received multiple briefs on it. We've been assured in the past that redundancy had been built in such that some anticipated problems could be dealt with and not get us off track. Nonetheless, I understand

that preclinical and clinical phases are inherently somewhat unstable. But I would hope as your GAN chart indicates that things really are happening in parallel rather than sort of a serial mindset. I would also say that the significance of this extends beyond simply the adenovirus vaccine. This really is a very visible marker to our troops and to others about what we are willing to get done on what sort of time schedule on their behalf. So with that preamble, any particular questions. Ms. Embrey.

MS. EMBREY: Adenovirus is not just limited to young healthy military personnel. Is it possible or has there been any exploration of perhaps cooperating with some college campuses who experience the same issues only don't admit it. Perhaps they might offer opportunities for clinical trials where our training schedules may not and allow us to continue on schedule.

DR. LISS: I think that is an excellent idea and actually we have explored that. But our strategy has really been to follow the label claims of Wyeth, which is limited to the military population. The FDA has attempted to allow us to use that strategy. We have identified a number of parallel populations and that's just one of them. But there's actually a couple of interesting other ones that I'd be glad to share with you

later. The problem is focus. And right now we think that we -- there is no red lights yet that stop us from using the military population. Another very critical part of using the military population as the target for this, since this is the intended use, is the fact that in a way they're not normal. You know, there are other vaccines they get and other routines that makes a typical college population a little -- actually significantly different. So we've thought about it but the guidance we've been getting from the FDA is that's not number one choice.

DR. POLAND: Let me ask Dr. Gray to comment. He's expert with this virus and spent a good deal of his career with it. Dr. Gray.

DR. GRAY: Thanks, I just have one question. Sometime ago we learned that there was perhaps a rate limiting step with respect to the serologic assays because of some problems at Walter Reed. Now you're moving to, you said, more than a thousand person clinical trial and I'm wondering have you resolved the rate limiting serologic assay problem?

DR. LISS: I think yes and really I wouldn't really call it a problem, although there was a problem with Walter Reed. I mean they weren't set up to be a large commercial type testing laboratory. But with

Walter Reed's help, we actually are in the process of transferring the technology to two different laboratories and they're actually competing with each other for efficacy. Not vaccine efficacy, testing efficacy and price. So I think that's been working really well in parallel. So while waiting for the trial to be fleshed out, we have qualified initially five different laboratories. They're now down to two for that assay and we are giving them, we're tempting them with larger numbers and their performance to larger numbers is one of the parameters that we are looking at. So I would say we have conquered that and again with WRAIR's help.

COL GIBSON: This is COL Gibson. COL Sun is going to be talking afterward, so he may be able to shed some additional light on that question.

DR. POLAND: Dr. Oxman.

DR. OXMAN: In long range thought are you in parallel doing any work to think of moving to MRC5 from DBI38?

DR. LISS: I'm so glad you brought that up. Well, low and behold, we talked about it at the last meeting. That was actually a quite high point. We had gone to another bio vial for virtual master cell bank. And as I mentioned perhaps earlier, I just returned in fact from Biolines in Scotland where we make the product.

I wish I could tell you exactly why, remember this is just a different vial from which another working cell bank has been initiated, but the DBI38 cells are doing wonderful. In fact, they are expanding to the point where we -- yesterday, we started two virus lots from a single cell expansion. In previous days, not to go into the gory details after lunch, but a single vial, we would often have trouble expanding that to a 100 T flasks. And now we're talking about 250 T flasks from single vial. For some reason, which I could tell you why, more robust and moving happily.

Now the second part of it, when we infect these cells, in fact the current yield of actual active type 4 - type 7 virus per milliliter is a little bit higher, perhaps within the statistics, but a little bit higher than MRC5 pilots. So currently we have about 20 to 25 years supply of DBI38 cells. Why this is important is that we believe from what we've heard from the FDA, not making a cell line shift at this time is less of a regulatory hurdle. Down the line maybe that's something we want to look at and certainly after licensing the optimization and other, something to do next, with this vaccine certainly would be open. But we're trying to focus on what we've got. So knock on wood, DMI39 cells are performing very well and we intend to keep the

course.

COL GIBSON: I have a question for CMR Russell about incidents of adenovirus. Have we seen any changes in DoD in recent months, year?

CMR RUSSELL: Kevin Russell with the Naval Health Research Center. We've done a review of about five years of data, 1999 to 2004 that was the years where the adenovirus vaccine wasn't in use at all. During those years we see a mean of about one case of adenovirus illness per one hundred recruits per week. That's a mean. Now if you look at those numbers alone, you'll see that over eight to 12 weeks of recruit training, you're going to get around eight to ten percent of your population, that have reported to sick call with a febrile illness. That's an important distinction. They have reported. They have chosen to risk the ramifications of going to health care, setback in training, going to medical rehab and have their illness looked at. Again that's the mean, so there are times when our rates get up to three and four cases per one hundred recruits. And during those periods, up to 30 percent of the given division might report to medical sick call. We have done other studies that show that one in two to one in three are about the proportions of individuals that chose to go to sick call when they have

a febrile illness. So again, further evidence that the ramifications for a recruit setting are extreme. Many recruits are suffering from this, having suboptimal training while they're suffering from it, and choosing not to go to sick call. So the advantages of getting that vaccine back are greater than even those numbers suggest. As far as what's happened since 2004, I can say that it continues at high levels, Great Lakes continues very high. MCRD San Diego which during the time of that five-year look, we had rates of .34. in the last year it's been one to four cases per one hundred recruits per week. Just a huge increase. Conversely, Lackland who did some major changes in the amount of recruits that came through, dropped to near nothing, and it has remained near nothing, even though they've increased their recruit numbers up again. So in a nutshell, there are still big problems throughout our recruit camps, but it's a moving target.

DR. POLAND: Again, our highest sustained continued interest from the Board perspective.

DR. LISS: We thank you for that and we want everyone to know that we feel very passionate. We want this to get done as well.

DR. POLAND: Dr. Oxman, do you have a comment.

DR. OXMAN: Quick question, of those febrile illnesses that reported to sick call, are there any samples that suggest what portion of them are adeno 4 and adeno 7?

CMR RUSSELL: Seventy to eighty percent of those that reported.

DR. OXMAN: Thank you.

COL GIBSON: For the record, it was 70 to 80 percent, from Kevin Russell.

DR. POLAND: Okay, thank you for filling in there.

(Applause.)

DR. POLAND: We have Dr. Wellington Sun report on the Adenovirus Vaccine Clinical Trial. Those slides are available right after CPT Midboe's.

COL SUN: Good afternoon. First of all, I'd like to thank Dr. Poland, Dr. Gray and all the members of AFEB for -- COL Gibson, for inviting me to give you this talk on from a clinical perspective the adeno project thus far at Walter Reed. I just want to make one mention, the problems with the assay, Dr. Gray, it was not at Walter Reed. I think that may have been a misnomer in that I think it was at the time, a two week delay, and since then we had that resolved.

Next slide please. So I'd like to go over

just briefly by way of background, vaccine development in general, and then go really into some of the details of the Phase 1 study with the new Barr vaccine that we have completed over the past year. And then compare that briefly with the Wyeth vaccine experience at Walter Reed and then some brief comments on -- from a clinical standpoint, points to consider from this point onward.

Next slide please. This is the context which I won't belabor it, but it's for any biological drug in terms of clinical development from Phase 1 all the way to a licensure, or Phase 2 post licensure. For the Adeno project and it's somewhat unique in the sense that because it is a previously licensed vaccine, we -- it was a thought that this process from Phase 1 to Phase 3 could be contracted. And in deed in may ways, I think the FDA has agreed with us that this could happen, but nonetheless, I think getting the regulatory requirements by 2005, it is not as easy as at “first blush”.

Next slide. So this is a slide I borrowed from Wyeth basically pointing out how the drug or vaccine development process has evolved over the last few decades. And as you can see, over the last four decades, the amount of time to bring a product to licensure really has dramatically increased, as well as the cost. And one of the -- for example, one of the estimates of bringing a

drug basically from the test tube to licensure amounts to as much as 800 million dollars. Certainly not the case for adeno, but nonetheless, this is a context I think for all drug and vaccine developments and we're really looking at the stage right here -- remember the Barr contractors led in 2001, and that's starting at the green shaded area there. So typically I think that's kind of the time frame we're looking at toward licensure.

Next slide please. I will go over then the results of the first Phase 1 study, conducted in the military population. This study was a collaboration by many different groups. It was a true team effort and with contributing members from all these DoD entities, as well as our sponsor. The principal investigators were Dr. Art Lyons at Walter Reed, and Dr. Jenice Longfield over at Brooke Army Medical Center.

Next slide please. So the goal for the first study was number one, to show that it is safe in a small number of individuals and then secondary objectives are to look at these immunogenicity, both in terms of seroconversion and serologic titers. And then we also wanted to look at the duration of vaccine virus shedding in the stool. This is important because first of all, we wanted to compare with the previous product, number one. And also, two, because the limit duration of basic

training, we wanted to ensure that this live virus is not shed beyond that period of time, which it could be secondary transmission in the community.

Next slide please. So the rationale for us picking the particular population that we use, were many fold. First, we wanted to try to replicate the basic training setting. We wanted to minimize, as I said, the potential for secondary spread in this kind of a setting. So we needed a -- hence, military population, because there the subjects are relatively cohorted or confined and there is no interaction with family members during that time.

Then we wanted to pick a -- because this is Phase 1, we are looking at immunogenicity. We wanted to select a population where we thought that there was low likelihood for active wild type 4 or 7 activity. And then we wanted to be able to recruit fairly large numbers quickly.

So next slide please. Before we actually performed the Phase 1 study, we selected a population at Fort Sam, the AMED school, 91 Whiskey School, which are combat medics. This is a school that the training, it's about 12 weeks, and it occurs right after basic training, so these soldiers have just completed basic training, so we wanted to know how many -- because they all to be

seronegative. We wanted to see, what is the seroprevalent population so we know how many people we have to screen to get the number of subjects that we needed. We needed a total of 60 subjects, that was our goal, with 30 placebo and 30 vaccines.

So this is what we found in preliminary Phase 1 seroprevalent study, and it was kind of not surprising that the adeno 4 seropositive rate was around 80 to 90 percent. Bear in mind that all of these soldiers had just come through basic training with this high level of disease activities. What we were a little bit surprised by though was the level of adeno 7 seropositives. There we measured close to 80 percent. If you can look at just the distribution, only two percent of those subjects, these were 99 randomly chosen subjects from a blood donation pool, only two percent had no serologic evidence of infection by both adeno 4 and 7.

Next slide please. So this is the basic design for the study. It is an eight week study and with one month to screen using the neutralizing antibody assay, the microneut for seronegatives and then vaccination on day zero, and then weekly follow-up up to four weeks and then the last visit at week eight. These are the collection points for serology, for throat and stool, rectal swabs, viremia. During the course of the

study any subject that presented with acute febrile illness were worked up by Kevin's lab for as well as the Walter Reed Army Medical Center clinical lab, for evidence of respiratory pathogen and adenovirus specifically. Our last follow-up which occurred six months after the vaccination date was required of us by FDA. So we actually telephoned or emailed subjects six months after the study just to see how they were doing. So this is basically the structure of the study -- by the way also, during the first week we asked for each of the subjects to fill out a diary. It's a double blind placebo control study.

Next slide. These are the inclusion/exclusion criteria. Basically these are very healthy individuals and no evidence of any active infection by HIV hepatitis B or C.

Next slide please. So looking at these 91 Whiskey candidates, we had to screen 407 to get close to the numbers that we needed. So really only 14 percent fulfilled the serologic criteria. We had to do this within a month and this is what we found. Again, this pretty much replicates what we found in the seroprevalent survey that I showed before. Again very low numbers of double seronegatives and relatively high levels of adeno 7, which was kind of surprising to us.

Next slide please. Here is a little historical context. This is the results of the study that we had -- I alluded to before, the 82 percent for the screening of the subjects, but these are two studies on them. The first one by Dr. Ludwig and the second one Forsyth, back in 1964 looking at this population was the preinduction. So these are troops entering basic training, and as you see, there the seroprevalence for adeno 4 was 34 and adeno 7 was 27. But this study was back in 1964, so it was after basic training or at AIT. Again here, relatively low incidence of adeno 4.

One caveat though, some of these assays, these were done by the microneut and I believe this one was -- this one was done by a tube neutralization assay. So not quite totally comparable but in our hands, those two assays corresponded very well in terms of there being concordant.

Next slide please. So this is the subject population for the Phase 1 study. It's a little busy, but I'll just walk briefly through this. At screening, this column of results again shows the -- remember these are people who we chose to be seronegative. So that's why we begin at zero. We had 47 percent only positive to 7 and 43 percent only positive to 4, and ten percent double negatives. So we thought that this was a

seronegative population. But during the time between screening to the actual day of vaccination, which you remember can be up to a month, we actually saw that there was seroconversion to adeno 4. You can see this here, 20 percent of them actually became positive from screening day to the actual day of vaccination. Because we do this, the vaccination titer afterwards. So there was no -- we could not have known at the time of day zero that they had seroconverted. So this was again, I think a little surprising to us that even in this population where seroprevalence in adeno 4 was close to 90 percent, there was actually still adeno 4 activity even within that ten percent who were seronegative. So we ended up vaccinating -- there were 30 individuals vaccinated with the vaccine and 28 total received placebo, for a total of 58 subjects. And of those 58, 54 completed the study. Four had dropped out for a nonvaccine related reasons.

Next slide please. So here's the safety results in a nutshell. These are all symptoms reported by the subjects that are over five -- well, over five percent, and placebo group and vaccine. The take home message here is that none of these sideeffects had any statistical significance -- difference between vaccine and placebo.

Next slide. Looking at the what we call serious adverse events. This is a definition, if I can just quote a federal regulation, any hospitalization is considered SAE, death and a prolonged hospitalization et cetera. We did not see any -- the only SAEs we saw were hospitalizations. So let me just go over them briefly. Between the time of the study from zero to 56 days there were two diagnosed pneumonias. One of those was in a vaccinee and one of those was in a placebo. The individual who developed pneumonia after he received placebo, turned out to have a wild type adeno 4, recovered. And then one case of ARD without pneumonia was hospitalized and again, this also was shown to be a wild type adeno 4. I think, you know, this may be the first study ever of an adenovirus vaccine where we actually were able to distinguish between vaccine virus and wild type, and through the use of molecular PCR.

There were two other SAEs. These were collected at the six month telephonic follow-up. In other words, these two individuals were hospitalized between the end of the study and their last follow-up. One was for an appendicitis, this was about four months after the vaccination. The other one was a MRSA thigh access in an individual who received placebo and again, that was about three months afterwards. So these are --

this one was not related to the vaccine certainly. So it's interesting to note that even in the small numbers, that there were two wild type adeno 4s in this population.

Next slide please. Remember we wanted to look at stool shedding. I think the only take home message here is that individuals did not shed virus beyond 28 days. So all of the shedding occurred in the antibody negatives, before day 28. Certainly well within the time frame for basic training. Important to know also that there were no adeno 7 isolated in any of the placebos.

Next slide please. So going now to the objective of looking at immunogenicity, this is just to show that the two populations between vaccinated and placebos, they were pretty much equivalent in terms of their sero status. As you can see, they are pretty well evenly distributed. Next slide. Here's the results for the immunogenicity. Here for adeno 4 and here for adeno 7. Now, looking at the only at the seronegative for adeno 4, the ones that were actually seronegative on day zero, and see how many of those actually seroconverted during the trial. Eight out of 11 or 72 percent and for adeno 4. And adeno 7, it was 64.7. So it was 11 out of 17. No seroconversions for 7, the placebo group. Now

here again, this is a -- remember in the beginning I said that we wanted to take a population where we thought adeno 4 would not be in circulation. Well, it turns out that there were three individuals who were the placebo group who did seroconvert and these were wild type, shown to be wild type to adeno 4. So this makes the seroconversion rate in the placebo group 30 percent. So this certainly complicates a little bit the interpretation of that 72 percent, because how much of that is due to wild type. I think that's one complexity when you deal with having to analyze this type of data in a setting where there is wild type infection. There is really no way to tell what percentage of that could have been due to adeno wild type. We could go back and look at the stool of the ones that were shed in these individuals and then see if it was vaccine or wild type. But we haven't done that yet. And that may be the only way that we could probably sort this out. I wanted you to just kind of remember that figure with that caveat and interpretation. Here are the confidence intervals for the two sero type conversions so it's with adeno 4 it's 39 - 94 and it was 38 - 86. Fairly broad ranges but these are small numbers.

Next slide please. So in summary, what did the Phase 1 results show? I think we achieved our

primary objective in showing that the adeno 4 and 7 vaccines are safe. There were no training days lost in the vaccine group. And all the -- the reported side-effects were no different from placebo. We show that the vaccine viral shedding was limited to 21 - 28 days. And it's actually -- it's very close the Wyeth vaccine where the shedding was up to three weeks. We didn't see evidence of wild type adeno 4 in circulation. That's an observation during the study. And then immunogenicity estimated at between 40 to 90 percent based on these small numbers of the Phase 1 study.

Next slide. So I want to just go over briefly a study that we conducted with the old Wyeth vaccine over at WRAIR and back in 1998. That was actually in anticipation of eventually having to do a comparison study. Unfortunately we didn't power that study large enough to be able to actually -- to do a true comparison. Furthermore, it was not a placebo controlled study. So there's some issues with that particular study. I think it does --- still it yields some interesting information because we use the same assay in looking at seroconversion. So that study was to characterize the antibody response and viral shedding from a licensed -- from the licensed Wyeth vaccines. And the study population was pretty much the same in the same

age group, except this was a group that we recruited from the civilian population over at Walter Reed. So these were actually paid volunteers instead of military subjects. The same inclusion criteria and pretty much the same schedule, though it only goes to 28 days, we're going to look at further out. And they recollected this serum urine, throat and stool and looked for adeno.

Next slide please. And again, this is -- remember civilian population is slightly different from what we saw with the basic trainees. Less adeno 7 and certainly less adeno 4 in that population before vaccination.

Next slide please. And I put this just as a reminder of the results of the Phase 1 study. And then what we found with Wyeth. These other symptoms are whited out because we did not solicit for those symptoms. It's not that they didn't report any, we just didn't solicit for them in our diaries. And these are the only symptoms that we solicited. Again, then you see that it's pretty, you know, based on these numbers, none of these really are all that different from the Barr vaccine, with maybe a slight exception of maybe there was a little more diarrhea with the old Wyeth vaccine.

Next slide please. So again, look at this with a grain of salt because these are two different

populations, although around the same age group, and two different vaccines. Just to compare -- just look at whether there are any gross differences in the seroconversion rate between 4 and 7 and the GNT's. So looking at adeno 4, you see that the seroconversion rate as I said, 72 percent for the Phase 1 study and 73 for the -- and this is using the same criteria for seropositivity. 73 percent with fairly close confidence intervals. Because this was not placebo controlled and we didn't look for wild type adeno 4, you know, and here we did, that could be a slight complication in really truly comparing the two. The GNTs were very similar. In general these are adeno 4 GNTs are lower than adeno 7s for the Wyeth vaccine. Now looking at 7 though, the seroconversion rate was 64 percent with Phase 1 and 92 for the Wyeth and in the literature actually for Wyeth vaccine, the seroconversion rate could be anywhere between 75 percent to a 100 percent. So certainly this was well within that range. And the 95 percent confidence interval for the Phase 1 study was 38-86. Nonetheless, I think this might be something that we want to look into in the future, as potentially maybe an issue to evaluate. One thing also, was the GNT for adeno 7 was somewhat lower than the Wyeth in this previous study. Again, bear in mind that these are not completely

comparable studies. Just enough for us to focus on for the next study.

Next slide please. So a reminder. As Kevin said before, most of the ARDs are caused by adeno 4 right now, and there's no adeno 7 since 1998. Somewhere between 60 percent to 70 percent of all viral infections are adenovirus.

Next slide please. So lastly, where do we go from this point. From my clinical investigator standpoint, I think that there are good reasons, I think, of why one has to go from a safety to immunogenicity and then finally you have to see -- I think that we are -- we looked at the Barr vaccine in terms of its safety. And I think in the next trial we certainly want to focus on the immunogenicity and then hopefully at the same time, efficacy. But safety, the dose, I think these are something that we really have not looked at and as Allan mentioned before, the issues of manufacturing consistency is very important. Being able to demonstrate that the lot we make is consistent in terms of it's inducing the immune response and the efficacy.

One issue that we have wrestled with is the issue of efficacy and correlate protection. Because right now in the basic training camps we see no activity caused by adeno 7. It's not possible to show efficacy

against 7. I think in our discussions with the regulatory or with FDA, I think they're very sympathetic to that and as a result of that, I think we are able to show efficacy based on a serologic correlate. So in this case, we will be looking at just merely seroconversion to adeno 7 to show that that could be used as basis for licensure. Whereas with the case of adeno 4, we had to actually show a reduction in disease. So these are very critical points in terms of design for the Phase 3.

Access to the military population. We plan on doing the next study at Fort Jackson and Great Lakes. Two of the largest basic training camps in the DoD so that we can have the kind of numbers and accessible subjects. And that logistically as CDR Russell and I are both well aware, could be challenge. We're trying to melt the requirements, the regulatory requirements and the statistical requirements with the training requirements of the population.

Finally, this is a question for DoD to answer. Knowing what we know about the Wyeth vaccine, what efficacy of this vaccine are we -- can be licensed. That's a question for the FDA. This is a question you. What efficacy does the DoD require this vaccine to have? Is it going to have to be as good as the Wyeth or are we going to accept something, you know, in the range of 80

percent or 60 percent? But I think this is a question that can only be answered by doing the study and seeing where the efficacy truly lies. But I think we need to makeup our minds, decide what we are going to accept.

Finally, I think it's going to be important even when the vaccine is licensed that we perform postmarketing surveillance as we're doing right now in the basic training camps. We want to be able to show on the ongoing basis the efficacy of the vaccine. And I think that's an important point, that we don't replicate the error that we made with the Wyeth vaccine in thinking that the disease had gone away because the vaccine was working so well.

And finally, all of these has to be basically negotiated and worked on together with our FDA colleagues and they have -- I think up to right now have been very, very sensitive to our needs and they have made, I think significant accommodations for us to be able to do the studies and still fulfill the requirements for licensure. And that's all I have. Thank you.

(Applause.)

DR. POLAND: Comments from the Board? Dr. Gray.

DR. GRAY: This is Greg Gray. I wonder if it bothers you that you're not seeing in all of your true

vaccine recipients virus in the gut? In other words, do you think there might be a problem with the coating that's making this less immunogenic or are they taking something orally that would conflict antacids with coating removal? Is there any suggestion of that?

DR. SUN: When they swallow the tablets it was probably on a fairly empty stomach because we had them there for a couple of hours before they actually swallowed a few tablets. So I don't think that the acidity issue is a problem. But I do agree with you, I think, you know, it is a small study. But I think there's enough there I think to -- that we will want to look at it more closely as to what is going on. I think to me, that is a reason for in the next study to really look at immunogenicity and more closely. We had -- are probably not going to want to do the looking at stool shedding in the large based retrial, because I think logistically it will just be very difficult. But I think the concern here -- what we're concerned about is absorptions or is infection, and that should be reflected in the immunogenicity. So I guess that's my long-winded way of saying yes. I see that as a potential concern.

DR. POLAND: Thank you, Dr. Sun. Is there either now or anything you can see in the future where the Board could be helpful in accelerated or continuing

progress here?

DR. SUN: I consider myself kind of an amateur in adenovirus. I've only kind of started looking at these issues and these clinical trials with adeno in the last three years. But the more I get into it, the more I realize that there is so much we still don't know about. Epidemiology of adenovirus in base training camps, why are disease rates right now, even though without the vaccine, so high, in general not as high as the prevaccine era? Why are we not seeing adeno 7? I think based on some preliminary molecular surveillance of data we have from our labs, that working with Kevin, that there seems to be some viruses at Cape May that has a unique signature and that seems to persist over the years. So I think there a lot of things we don't understand about adeno, and I think in trying to recreate the vaccine has actually highlighted our ignorance. So I think that there's a lot to be learned. I would like to, as a researcher, I think it's important for the Board perhaps to recommended that more basic research done in the adenovirus in the military setting.

DR. POLAND: Thank you. Oh, one other question.

COL GIBSON: COL Gibson. Looking at the GAN chart it appears as though you're phase -- you're

obviously in a planning stages for the Phase 3 trial. Do you have a date or an estimated date where you are going to start enrolling subjects?

COL SUN: Where we are with the Phase 3 trial is at the -- we had this FDA meeting back just a few days ago, November 30th, where I think we got a fairly good idea of what it is going to take in terms of sample size and end point and so on. So in the next stage we plan on putting that into -- actually writing a protocol. And then we have a formal end of Phase 2 meeting with the FDA sometimes in January. I think there we will need to get the FDA to buy off on our proposed protocol, and I think from then, from that point on, actively -- we are certain about what is required for the Phase 3 -- Phase 2/3, then I think we could have a more reasonable estimate as to when that trial can start. So I am not trying to hedge, but I think there are so many, at this point, short term uncertainties about the timing. But I think it's fair to say that we -- Phase 2/3 trial, I think mostly likely will be in 2006.

DR. POLAND: Thank you. Dr. Oxman.

DR. OXMAN: Two part question. What assay is the definitive assay you're using for the serologic tests?

COL SUN: We're using the colorimetric

micron neutralization.

DR. OXMAN: Do you have sera frozen from the efficacy trials that were done with the Wyeth vaccine which certainly do not use that assay, because you're talking about, in answering the advance question, you're talking about using the antibody neut assay as your definitive measure of success, and you're not paying as much attention to the duration of shedding and in fact there may be quantitative aspects of immunity that you're missing. And I wonder if you have anything to compare to the laboratory base of the Wyeth vaccine?

COL SUN: The 1998 study of the Wyeth vaccine, we do have those sera in our archives, and we could go back and do that comparison as you mentioned. We've also, actually -- this is -- I don't know, maybe many Board members know about Dr. Leonard Vin, but he's been at Barr for over 50 years and his lab actually does the assays. He's looked at comparison of the plaque neut versus the microneutralization as well as the tube neutralization assay. And actually have found that the results are fairly closely parallel. So I think certainly the microneurtralization, because it's formatted has a much higher resolution.

So I think that we can do that study, comparing the Wyeth vaccine sera with the Barr vaccine

sera, but I am not aware that we have any other sera from pretrials previous to the one that we did in 1998. Those sera I don't think are available. Does that answer your questions?

DR. OXMAN: Yes.

DR. GRAY: This is Greg Gray again. Just perhaps for the benefit of the Board or everybody else involved here, there was recently a study published in Clinical Infectious Diseases looking at UK recruits and they had a very high proportion of their febrile respiratory illness due to adenovirus and so maybe there's potential there, not only to expand, as Ms. Embrey suggested, to the civilian populations, but to the military populations of other nations.

DR. POLAND: Okay, thank you. We'll move on now to a different topic. We're changing gears to injuries. Dr. Paul Amoroso is going to provide us a briefing on paratrooper ankle injury intervention and evaluation. His slides were handed out and I don't think we're -- so you do have the slides up.

Dr. Amoroso, thank you for coming.

COL AMOROSO: Thank you, sir. I very much appreciate the opportunity to come and speak with you today. I am going to really tell a story. It's a story of injury control in the Army that starts about 15 years

ago, and is still unfolding today. It is fortunate that we're here at Fort Bragg, the heart of Army Airborne to give this talk. It's a talk about how to prevent injuries among parachutists.

Next slide. Before we get into that, I think to help you also gain an appreciation for what you might see tomorrow if you get the chance to go and observe a parachute jump, and also to put a small but very important injury problem in perspective for the presentation that will follow by Dr. Jones, I thought maybe I'd start with an overview of actual parachuting so you can all have a good grounding of what that's about.

Next slide. This is the military parachutist. You'll notice right away that he's got an awful lot of stuff with him. And it really depends upon the mission that they're going to engage. In a training flight, they wouldn't take this sort of stuff, but he's probably got a 40 pound pack on his back that has his main parachute you don't even see, the reserve chute here that weighs a little bit less than that, and his main pack that is going to be his ruck sack that he's going to carry all of his gear for how many days he might be out on a mission. And depending on what kind of weapon system he's involved with, he could have any manner of things that he could carry in addition. So it is very

cumbersome, very hard to get in and out of an aircraft, as you might imagine.

Next slide. Here is a number of soldiers here at Fort Bragg getting ready to get on the airplanes. They've got their game faces on and they are ready to get on the mission and get going.

Next slide. This is how they get packed into the aircraft. You can see that there is not much space in there. If it is a training mission that's here at Fort Bragg, they may not be on the plane very long, just takes getting up to altitude and getting them out over the drop zone and getting a green light and going for it. But if they were going to Panama, they are going to be sitting under these conditions for quite a long time.

Next slide. When the conditions are right and they're over the right spot where they are going to be let out, they're given signals both audible and visual to stand, and they will go gangbusters out those doors, oftentimes both sides at once.

Next slide. This is what a typical distribution of parachutists might look like. You'll might be able to pick an airplane here and there in the picture. The difference being that most of the time it's at night and you wouldn't be getting this picture at all, but this is a typical mass tactical operation, many, many

people can get on the ground very quickly.

Next slide. More typical pattern that in training, such as at the Airborne School, is one of the things I will be talking about a little later, the pace is slower, it's more orderly, the spacing is controlled and where they land is also well controlled.

Next slide. Here's an example of an individual just before landing. Some of that equipment that you saw that other guy carrying, they will pull a lanyard and release it so it doesn't ride in with them. That's good because it reduces their weight and their speed of decent slightly before they get there. It also a place where things can go wrong. If you don't do that appropriately, you're going to land heavy or you might land on it, or you might get encumbered by it.

Next slide. This is a slide at the Airborne School. Again you can see the wide distribution, very nice flat landing space. This is a controlled situation, very much like you would see in the training environments such as at Fort Benning.

Next slide. This slide, technically not of great quality, but what it does do, this is an actual problem up here with the chute, a pair of jumpers getting -- interfering with each other. There are many places in the course of a jump where an individual can get in

trouble versus getting out of that aircraft, they can get hit, they can get tangled, they can get beat against the side if they stay that way. And then all the things on the way down; their chute not opening, other jumpers are their main hazard. And this is a case where one jumper floats over the other and steals the air, and just -- that person will just drop right underneath the person below him, and then the same things just happens, and it just leap frog all the way down. So this is a particularly hazardous situation. And one that a jumper only has partial control to avoid that.

Next slide. Here's the ouch. This is the worst part of the experience for almost everybody. This individual is making what is called a parachute landing fall. This is a procedure that's been developed over many, many years of jumping, since the early '50s. Essentially a person tries to distribute the force of impact over five different points in the body, so that it distributes that G-force.

This, as you might imagine is where most injuries occur whether that be related to something that occurred in descent or at the exit, nonetheless, impact is where most of the problems occur.

Next.

Once the person is safely on the ground, they

still have to get free of that chute. People have died and been seriously injured. It still happens today where that chute just takes them somewhere that they don't want to go, drags them across something or into something that they don't want to be.

Next slide. So that's a brief overview of who the characters are in this story. What I would like to do is give you just the basic plot. It starts with problem identification. We were told that there were high injury rates among the parachutists and asked to assist. That led us to some preliminary scientific investigations. Ultimately to the development of intervention, the parachute ankle brace, randomized intervention trials with its difficulties and challenges but nonetheless successful. Along the way some additional studies were accomplished. The intervention got fielded. Unfortunately there was some decay as often happens over time. The intervention maybe is believed no longer necessary or just too difficult, too costly to continue with. And of course the position of having to gather additional scientific evidence and to do an evaluation study. The piece that so rarely gets done after intervention trials are, whether it be civilian or military. And that brings us back to the beginning and also to the present. You'll see when we get there.

Next slide. So we start in 1991 and I was tasked to do my first field study, and sent down to Fort Benning to investigate airborne injuries among the Airborne School. Clearly early on we found that injuries usually occur on landing, and mostly to lower extremities.

Next slide. In 1991 I surveyed one class of Airborne students. We took volunteers there and found that about six and a half percent were seen for some form of an injury in the clinic or in the emergency department. Almost 70 percent of those were the lower extremity. That gave us an idea of what we needed to know for our future studies in terms of power.

Next. We also had at our disposal the data that the Safety Center collects. Routinely as injuries occur and time is lost from work in the Army, it's a requirement that reports be sent to the Safety Center. They have a code in that data system that involves tactical parachuting, so they were easy cases to find. The data is very good for qualitative purposes, not so good for rates, since the reporting is somewhat valitional on the parts of the unit, but there were thousands of jumps in there that we could evaluate.

Next slide. The key thing to see, this was a study that spans about a decade's worth of data, a

little over 4,000 cases, but the main thing I wanted to point out was that for men at least, 60 percent of the injury is lower extremity, much higher for women, closer to 70 percent.

Next slide. In order to look at cause, and that's not our usual traditional definition that's known as cause, but what I was looking for was the proximal reason that the injury occurred. And in order to get to this, we had to review many, many of the narrative summaries that are provided. That rich detail allowed us to go look and see where in the sequence of the jump the injury occurred, be it aircraft exit or something in the air, whether it be a malfunction or some interference or some problem that the soldier themselves may have done in terms of canopy control. Sometimes it's something on the ground; a truck, a stone, a rock, whatever, that they land on. More often than not, it's that parachute landing fall. It's a very complex maneuver, it's difficult to do under all conditions and especially for women, it appeared that that was a major problem. This is a case of blaming the victim, which we don't like to do in injury control, but nonetheless, it seems report after report indicated that that's the place where people get into trouble.

Next slide. Development of an intervention.

This is a parachute ankle brace. This idea was proposed -- we had a proposal brought to us by an orthopedic surgeon by the name of Jack Ryan who had been at West Point and worked with West Point cadets, athletes, mostly basketball and found that bracing was very effective for those sort of injuries. So he proposed that we take this to the parachutists. So Aircast Corporation, which makes a lot of medical braces had this brace and customized it for that purpose. It fits right over the boot and there were some other designs, an inside the boot brace, which had a few problems that weren't so much at play with this brace; fairly easy to put on. You can run in it, you can walk, not quite to the degree you could without it, but nonetheless, it didn't really restrict the individual. Relatively inexpensive; fifty bucks then, about sixty bucks now for a pair, and reasonably comfortable.

Next. Our next step was a randomized intervention trial. We designed the study and planned it for right here at Fort Bragg. It takes a while to get something like that coordinated, and it took us several months to get things set up. The day before we left, our advance party was already down here with the truck and the equipment, I got a call from division surgeon said, hey, you can come, but we are not going to be here, sorry. So we were left at home kind of wondering what to

do with ourselves. We probably would have been many months before we could not only have had them back, but also reconfiguring into their training schedule again.

It didn't take us too long to realize that maybe there was another place to go. So we chose the Airborne School. There were some pluses and minuses to doing that. Within the Airborne community, this is not quite what they want to see, because students are different, the rigors of jumping in training are not quite the same. But it had an advantage that it's quite a controlled environment. And even though the injury rates were lower, we had the structure that we could take advantage of in terms of doing a randomized trial. So it turned out to be rather fortuitous.

Next slide. We got down there and enrolled four consecutive classes, volunteers from four consecutive classes, 777 volunteers, almost 3700 jumps. We did a pre-survey that allowed us to get prior health and injury history as well as health hazard information. We did a survey after each of the jumps. We did full medical records review and all of the injured soldiers were examined by an orthopedic surgeon.

Next slide. What we got with a fairly rigorous study, not highly powered, nonetheless, we were still able to demonstrate that the expected result was

there. Mainly that was that we would be able to prevent inversion/version sprains. And this gives the basic data on that. We didn't really see any other injuries that were unexpected or worried about that many people thought, well, if you prevent the ankle from getting injury, you'll get upstream injuries, in the knee and the hip and whatnot. We didn't see any evidence of that.

Next slide. We came back to Fort Bragg with the intent to do a second randomized trial, because they really felt that they needed a study in an operational environment. That turned out to be next to impossible to accomplish here given the training schedule. And while it was consistent with the results we got in the previous study, we really didn't have much power to make any firm conclusions. A couple of other studies happened since then with the Rangers. Both again consistent, not finding any unexpected injuries and showing a clear benefit to the brace.

Next slide. Within weeks of finishing our study at Fort Benning, the Airborne School Commander was quite convinced that this is something that he should just make policy. And in fact, that's what he did. So they more or less continued to use the braces indefinitely after that. We had used some traditional Army methods of assessing the cross benefit of bringing

an article of equipment or clothing into the inventory, and based on that, we came up with a projected cost of about two and a half million a year, just based on the school's use of the braces.

The army type classified the braces, which means it gets a stock number. That meant anybody who had money could buy it. And shortly thereafter, it seemed like it took forever to me, but I was later told that it actually went quite fast, 40,000 pairs of the braces were purchased and sent out to the 82nd Airborne Ranger Battalions and the like.

The use of the braces wasn't really required for the 82nd or the Rangers, but various pockets and sub groups of the pockets and subgroups of those populations did in fact use them.

Next slide. The Airborne School after about seven years decided that maybe they weren't going to use the brace anymore. They gave us a little bit of warning about this, but not much. The reasons that they cited were that the brace was too costly, and indeed perhaps they were from their perspective. I don't know what the budget was for the Airborne Battalion, but I think the braces were costing about $70,000 a year and I'm sure that their budget wasn't more than four times that. So from that perspective, the 2.5 million dollars of

savings or not, they didn't really recognize that difference. They felt that their injury rates were already low. there was some other anecdotal concerns that had been raised around the Army. The same things that had surfaced before were coming back and now they had more reason to listen to those perhaps.

Next slide. There was some anecdotal concerns that arose from some individuals here. In particular, an orthopedic surgeon here had reported that he had repaired multiple blown knees, and while he admitted that not all of these individuals were wearing braces and in fact, he didn't know which ones may have been wearing braces for sure. The reason -- the story that feet had been caught in the risers was troublesome, because if indeed if the boot gets caught in the risers, that opening shock is such a torque and a rapid pull that it'll just blow the knee right out. So that's potentially a very serious injury. Whether it could be proven or not at that point, the brace, whatever the profile of it may be sticking outside the boot, logically could in fact increase the likelihood of an entanglement. So we couldn't really make an argument against that based on the data we had. Meanwhile, the second and the Third Ranger Battalion had also some anecdotal things, one of which, you know, a brace got caught in the risers and there was an ACL tear

associated with that. And there was another case where someone's foot with the braces on got caught in the inversion of a second jumper. While there was no injury, that sort of also caused a lot of problems and upset.

Next slide. We were faced with having to generate some more data or to accomplish some pretty sophisticated cost benefit analysis. Sprains and fractures are duty limiting and they can be quite serious, can result in career termination for some individuals in the service. They usually result in full recovery. On the other hand, an entanglement may be very rare, it could happen one in a million jumps, one in ten million jumps, but if it leads to death, that's a problem that couldn't advise them on how to weigh. That becomes a complicated risk benefit, no matter who's making it.

So there are many ways to look at it, and we really as a medical research institution couldn't really make a firm recommendation about exactly what they should do yet.

Next slide. So what additional research was possible? Many proposed a randomized trial. That really would be impractical to get the kinds of things we thought we might need to detect. Prospective studies would be costly and technically challenging. If we were to do something on the ground here at Fort Bragg, that

would require many individuals here for some prolonged period of time, because the data collection would require some verifying. Most of all, that would take some time. We would really have to wait until enough jumps accumulated that you could really make a demonstration about these relatively rare events. A retrospective study was possible, but that might also have been technically challenging.

Next slide. It happens that I had created and managed a large administrative database, including outcomes such as hospitalization and knowing that it would be possible to link the student rosters at the Airborne School to this data, that was the approach we next took. It turned out from about 1985 until about 2002 when that study was done, there had been about 220,000 soldiers who had completed Airborne training. And that's well over a million jumps. And there really hadn't been a series as large as that before then, especially with individual level data that could be controlled for so many covariates. Virtually all of the hospitalizations would end up at the Fort Benning Hospital because the drop zone is there at Fort Benning and any injury that occurs there is going to get taken immediately by ambulance to the local hospital. We could detect those hospitalizations in a relatively unbiased

way, because the data collection is independent of anything that had to do with any of this.

Next slide. The complicated part for us was that the rosters of the soldiers that went through training existed electronically only from about October '95. This by no coincidence is when I started asking for that data. After that they kept the rosters, but before that, they would just make their own printout and stick it in a file cabinet so they could prove who had done the training. So we actually had to go back and make scans of these paper rosters and have somebody enter those social security numbers into a data base so that we could do the study. That took us a good half a year to do. Once we accomplished that, we now had a comparison of 127,000 students that had jumped in school prior to the brace, 68,000 that jumped during the brace protocol and then about 28,000 after. So it was a nice little natural experiment. We had one period here in October '93 when we did the randomized trial, so that quarter was a little clouded by not really being able to detect who was actually wearing the brace. So we just excluded that from the analysis.

Next slide. This is a chart which shows the hospitalization rates for the students over the course of time from beginning the study in 1985 until the end of

2002. The one thing that jumps right out is the trend of overall hospitalizations for ankle injuries is down, and that's typical for most injuries now, as we manage more and more of them on an outpatient basis. But what stands out more is perhaps a difference in the slump of these two lines overall and then during the brace protocol. So once the braces came into existence, boom down came the rates and then once they came back, it went back up. We had an odds ratio of about 2.4 for the period prior, and a little bit lower, that might be expected since rates are trending down a bit, about 1.7. But a clear trend and a clear difference across all the different types of ankle injuries, whether they required surgery or not.

Next slide. So is that the end of the story? Well, based on the weight of this evidence and some high level interest within the Department of Defense, looking for ways to reduce injuries, the braces have now been introduced, as of July 2005, the Airborne School at least is using them. We have another conditional evaluation study underway at USARIEM. We now have yet another period of brace use to make a comparison. We also have piloted the use of outpatient data where cause information isn't present, but nonetheless, we have very good time markers, so we can tell where people are and what their visits are made for. So we think that that's

going to work quite well. There are scads more in congress based upon outpatient data. Fort Benning is also doing a survey of their own and the preliminary results from that, completely consistent with what we've seen so far with the marked reduction in injury, ankle injury.

We'll soon extend to the rest of the Airborne community. That is right now just sort of waiting on funding and these other steps to take place.

And I think Bruce Jones will be talking quite a bit about some of the global efforts that are now underway within the Department of Defense, so I won't go into detail with that.

Last slide. I'll be happy to entertain any comments or questions at this point.

DR. POLAND: We'll start at that end and work our way down.

CPT NAITO: Neil Naito. Is there any seasonal variation for injuries during Airborne training. I noticed when I did jumps during the summer, I landed like a sack of potatoes and during the fall and winter it was much softer landing.

COL AMOROSO: There is and I couldn't tell you the precise details but a couple of factors come into play. The density of the air certainly affects the

descent rate and the hardness of the ground. And with the exception of some of the operational units jumping in snow, they have basically zero injury rate.

CPT NAITO: One more question. I noticed when I went through training that the land based training, I actually thought they were more dangerous than the actual parachute jump. Are injury rates higher during the land based training phase? And also, do people wear the -- students wear the brace during that time or are there any different injuries?

COL AMOROSO: The ground -- the Airborne School for the Army is divided into three phases. There's like a ground week, a tower week and then a jump week. The injury rate, surprisingly in the first couple of weeks are really remarkably low, especially in comparison to the jump week. But there are some, and many of those individuals wash out, don't get to jump. Our primary focus has been of course on the jumpers. But there are some injuries and those apparatus are very dangerous, at least you know there is certainly plenty opportunity for injury, usually not serious ones.

DR. POLAND: Okay. Let's keep moving in view of the fact that we're quite behind.

DR. LEDNAR: Wayne Lednar. I am struck on your slide 32, which is the graph, between 1985 and 1993,

before the braces were introduced. There is really quite a variation in injury risk. As a matter of fact, at one point the risk was cut in half from where it had been. All of this is prebrace. I am wondering if you have any clue as what might have contributed to that differential injury rate because that might be another one of those messages to maybe force at this point, in addition to the brace. Because something about how the training was being done seem --

COL AMOROSO: I really don't have an explanation for it, but it's certainly worth looking into. I will do that, so I can get you an answer.

PROF. BAKER: Sue Baker. Very nice presentation. I'm interested, since you mentioned that $70,000 a year was more than they could afford even though it might be saving millions or a lot more than that, the general problem of the fact that the people who have to pay for whatever the preventative measure is, their budget doesn't get the money that comes from saving injuries and so on. Have you any suggestions as to how that problem can be alleviated because that is often crucial to having cost benefit analysis making a difference.

COL AMOROSO: Yeah, that is something that we recognize in this new implementation phase is that we

had to get the braces out of the budget in the unit level. And so there are various ways explored to do that. It gets complex within the Army system to have property assigned different places. I think we will get that solved and in fact it won't be something that comes out of their budget, even if you give them the money at the end of the year or during the year, they still have to deal with the fact that that's part of their budget, and they're going to want to spend it on something that they consider higher priority. So the only way to solve this is to get it right out of their hands. And that's what we're attempting to do and I think we'll be successful.

DR. POLAND: DR. Halperin and then Dr. Lemasters.

DR. HALPERIN: It's a very nice case study. The technology looks like it is from the 1930s. Why don't they use these glider shoes which would seem a little bit more controllable and avoid a lot of the problems that you describe are a problem.

COL AMOROSO: It's a two-edge sword really. You don't want to have people flying around. You want to get them on the ground quickly. From a tactical standpoint, the purpose of it is to get a mass of people on the ground immediately. If you give the soldiers a

chance to fly around, that wouldn't work. Now many things have been explored as far as decreasing the descent rate, especially just before landing. In fact there is a new parachute system that will be fielded in a few years. And by the time it does this, it will all be moot, because the speed of landing will go from 21 feet per second down to about 18, and that's enough to make a huge difference. But the short answer is that you can't -- that would be worse actually, the opportunity for collisions and entanglements would just be huge.

DR. LEMASTERS: Grace Lemasters. When you plotted the graph in your ankle injuries, did you also plot what was going on with the leg and knees to see, during that period of time? Did you notice any difference?

COL AMOROSO: No. We took a careful look at that, because that was going to be the main reservation of them even looking at our work. That was the main thing we set out to prove or disprove, that there wouldn't be an increase in any hip or any injury, really.

DR. LEMASTERS: So they didn't increase much?

COL AMOROSO: No.

DR. POLAND: Just as an aside, it's very interesting how people believe what they want to beleive. Dr. Jones.

DR. JONES: Bruce Jones. I have been working with Paul on this for a number of years. This is interesting not just in the science at least prevention, but also how they are obstacles in what we believe in getting things used, that really prevent injuries and don't cause other injuries. Paul and I have been hearing about a report that the Airborne Board -- test Board here at Fort Bragg had done that showed that this brace caused injuries. Well, this summer I happened to jump with a group. It was my only jump ever, but it was a lot of fun. Anyway, that's another story. And I was given a copy of this report and I was very anxious to read it. I was tempted to read it while I was driving home, but I didn't. I waited until the next morning. I searched for the evidence that the brace caused injuries and there was no evidence. The report that I was given that we had been hearing about all of these years that was provided to me by a parachutist, really showed the contrary. It said that the Board decided that it was safe and that it was well accepted. So what you hear, you know, through the rumor mill, frequently persuades you the truth is contrary to the facts you believe, and even the evidence that you feel that you hold in your hand sometimes is different anyway. So I thought that was very interesting. That after all of these years we found it

just as we start another trial. But we're still confronted with that culture and that belief that the brace causes injury.

COL GIBSON: Real quick question. On your original cost benefit model did you include training time lost from hospitalization?

COL AMOROSO: I don't believe so. It's a complex model and really we didn't have control. It is sort of a black box thing that exists in the health hazard assessment area. I think that might have been part of it. I really don't remember. It has been more than a decade since that was done.

COL GIBSON: I get fairly good traction with basic training recruitments by including training time loss in a cost benefit model if that....

COL AMOROSO: This work would definitely benefit from a more rigorous cost benefit analysis and that was really not what that was.

DR. POLAND: Dr. Amoroso, thank you very much.

(Applause.)

DR. POLAND: Dr. Jones is coming up. We are working on trying to get this heat level down. For those of us from the Midwest, it's intolerable.

Dr. Bruce Jones is joining us today with an

overall injury update for DoD. His slides are located under Tab 7. Bruce, welcome. Haven't seen you for a while. Anything you can do to help us catch up too, would be appreciated.

DR. JONES: Great. I will try, although actually the last time I gave my talk it went 33 minutes. I'll try and parse my words here. Can you hear me out there?

I am honored to be here, Ms. Embrey, other Board members, COL Gibson. The last time I was here I presented a report to the Board that was the work of a committee of the AFEB that I co-chaired. The title of that report was Injuries in the Military, Hidden Epidemic. The epidemic is no longer hidden, but there is a lot of work left to do. I would like to talk to you about an approach that I think is like what we need to do. I am not sure that it's the final answer, and a lot of the insights that I gleaned into the possible process that could be employed has been gained from my participation on the military training task force, which is task -- one of eight task forces under the defense safety oversight counsel.

Next slide. I'll give you some background on the Defense Safety Oversight Council, the military injury metrics that are sort of governing or tracking

what we're doing. I'd like to give you an overview also of the magnitude of the problem of injuries looking at deaths, hospitalization and outpatient data from a variety of sources. These have been pulled together from a series of briefings that have taken place at various levels of the Department of Ddefense over the last six months or so. So they're not all completely consistent with each other. They're consistent internally within any series of slides, but not necessarily across them.

I'd like to then talk to you about a process for setting injury prevention priorities which I think is extremely important if we're going to be successful in the long run, then talk about a few counter measure that can be recommended out of that process and then talk to you about what I think we can conclude from what you will have seen and some possible future directions.

Next slide. The Defense Safety Oversight Council had its origin in the -- a memo from the Secretary of Defense challenging the services to reduce accident mishap rates by fifty percent. That was in May of 2000 and they were anticipating that they could do this within a couple of years. That hasn't happened but lots of progress has been made. In June, the Defense Safety Oversight Council was chartered by the under Secretary of Defense for Personnel and Readiness, Dr. Chu

who chairs the Oversight Council. There were eight task forces under the DSOC and there were four metrics established to track overall progress.

Next slide. These are the eight task forces that fall under the DSOC, deployment and operations, military training, which I'm a part of, aviation safety, private motor vehicle accident reduction, installation industrial ops, worker's compensation and then enterprise information system for injuries is pulling together safety, medical, and other data. And an acquisition and technology task force. These ones up here have their own metrics. I'm not going to go into all of them because it would be just too difficult.

` Next slide. This is the metric that is shown at the DSOC meetings and other meetings where we are tracking my task force. I'm not the chair of that, but I'm a member of it. And I chaired the data collection and metrics committee. And this is one of the biggest problem areas. I mean, not only hasn't it met its goal, but military injury case rates are going up. And the case rates are a combination -- what it is is it's the sum of individuals who have had one or more hospitalization or one or more day of quarters or more serious injuries, per hundred, per year for each of the services. And you can see that after initial apparent

success in 2003, that rates have been going up, probably due to increased operational tempo and redeployment and efforts to maintain training and also recover from your prior deployment and get ready for your next one.

Next slide. What I would like to do now is show you medical data on deaths acquired for AFIP in early 2005.

Next slide. As you can imagine, hospital deaths, combat related deaths are the leading cause right now across the services, but 2004 was the first year that this had happened in some time. Accidents account for the second most number of deaths, and in fact throughout virtually all of my career, 25 years in looking at this, accidents have always been the leading cause until this year. Suicide was third, natural causes fourth and so on down the line. But accidents, even during combat were right up there.

Next slide. Now this looks more specifically at causes for both injuries and disease, again hostile action is the leading cause, and I'm going to focus on this column over here for the sake of time. There's lots of interesting things to observe in differences between the services and not unexpectedly when you look at hostile action, the Air Force and the Navy have fewer and a lower percentage of casualties. But hostile action is

one. Motor vehicle crashes as a specific category of cause is next, followed by suicide and then some medical problems. And then we see the next four or five are all about two percent of total casualties and they're different injury categories, aviation.

Next slide. Now looking at hospitalizations, we're going to see a different picture. As you saw, there are only barely over a thousand fatalities DoD wide.

Next slide. There are over 50,000 hospitalizations and what we see is that injuries and injury related musculoskeletal conditions, the yellow are the musculoskeletal conditions. Things like stress fractures and Achilles tendonitis account for about 25 percent of hospitalizations. The next leading cause is mental illness at about 18 percent, GI at 13 percent. So injuries are really the leading cause of hospitalizations.

Next slide. Now, knowing that you've got a problem and injuries are a big problem, isn't enough. You've got to know what the causes are. These are acute causes. We can break them down with the medical data into somewhat finer categories, but we really need safety data to get down to the real details, but these can give us some idea where our priority should be.

Across the services for a number of years the leading cause of injury hospitalizations has been falls slips and trips. The vast majority of these are falls. For DoD overall, about 23 percent. If we look at the next leading category, guns and explosions, but that's due to the Army and Marine Corps. This has never been in the top ten before the last couple of years, so this is directly related to opstempo, and these are noncombat related, certain material handling aspects of ordinance and weapons training and so forth. Then land transport, which is always in the top three or four, followed by -- and here's what's different. The war is not the leading cause of hospitalization. It's fourth overall at about ten percent, followed by sports. And we're just looking at the top five causes here. We could list about 25 or so.

Next slide. If we look at air medical evacuations, we have data from the TRANSCOM. Next slide. This is only Army data. The bulk of the data from the theater is in fact army data and then marines. And what we see is that the purple is nonbattle injuries, yellow is battle injuries and disease. This is a little different than the other slides. If you sum the total of the nonbattle injuries, it comes to about 35 percent of all the medical evacuations for the army, and due to

nonbattle injuries. And then battle injuries make up about 15 percent. And then we see things like ill-defined conditions, digestive disease at about nine percent.

Next slide. Now looking at the causes is very interesting because it's so similar to what we see during peace time. Falls and jumps are the leading cause right now of nonbattle injuries, about 18 percent, 19 percent. Falls not from a vehicle are at the bulk of them, but it's interesting that three categories making up about seven percent are falls or jumps from a stationary vehicle. Probably a preventable problem. Many of them the solutions could probably be engineered. The third leading cause have been sports and physical training followed by military motor vehicles, lifting, pushing, pulling, and the others that we see here.

Next slide. Before we look at the outpatient data, one of our big problems is is that the bulk of our injuries are seen on an outpatient basis and many of these are serious. 28,000 fractures of the lower extremity here, a similar number of upper extremity fractures, really duty limiting injuries are treated on an outpatient basis. Many days of manpower lost. We have no cause coding of the outpatient injury, so we do not have a good foundation, except through research into

what the causes are.

Next slide. But this is where the bulk of the problem is, out of 6.6 million roughly, outpatient visits a year, two million or so, 1.9 million, 1.8 million, somewhere in that range, 30 percent of them are injury related conditions. The next leading causes are vague signs and symptoms of those ill-defined conditions you've seen before, eleven percent, respiratory at ten percent.

Next slide. If we look at the overall rates of categories of these injuries compared to a subcategory, overuse lower extremity injuries, we get some sense of where these are coming from. The overall rates of outpatient visits are about a thousand per thousand service members per year, and 50 percent of those are overuse lower extremity injuries that research has shown are primarily due to running and marching. So our -- the foundation of much of our training.

Next slide. This is a slide -- this is the type of study we need to do to get at causes at this time. If we had cause coding of outpatient data, we could do this on a routine basis. This is a study from Fort Reilly, Kansas between 2001-2002 medical records were done of a hundred percent of the battalion, included records on 768 soldiers who were at Fort Reilly that whole period of time. Twenty-nine percent of the

injuries were physical training related, 80 percent of them were due to running. As I said, by the medical records, followed by sports, field training, motor pool activities, repairing vehicles and so forth, and the military vehicle crashes with POV. So you see widely different causes as we go from deaths to hospitalization, outpatient.

Next slide. This is the DoD injury pyramid constructed from the data you've seen previously. For every death there are about 30 hospitalizations and almost 4,000 outpatient visits, 40 to 50 percent of those require a day or more of limited duty. So we are talking about huge numbers down here.

Next slide. With a problem this large and complex and involving such great numbers at the base of the pyramid as we saw 1.9 million clinic visits among roughly 800, 900,000 service members annually. We can estimate about 25 million days of limited duty due to these a year. And since the causes change as we go down the pyramid, we can't just focus at one element. We've been focused primarily on deaths. And we've set our priorities on preventing aviation and motor vehicle crashes with very little attention paid to things like falls, which actually turn out to be quite big. We need, I think, a systematic evidence based prevention process

based on the magnitude and severity of the problem, and the preventability of the problem.

Next slide. We engaged in such a process back in 2002 at Johns Hopkins University. Professor Baker was part of that initiative. We had eight military, four non -- eight Army, four non-Army staff from Johns Hopkins, the Air Force and the V A. We reviewed and discussed injury data such as you just saw and talked about what we knew of evidence for prevention that was out there. We brainstormed some additional criteria. We grouped the criteria and then we applied the criteria, to the rank 25 causes.

Next slide. The five categories, main categories were -- first is it consistent with your mission. Next is what's the importance of the problem to force health and readiness. How preventable is the problem, how feasible is it to implement the program, and can we evaluate it. Is there a metric we could use.

Next slide. We came up with a score sheet. Each of those five categories had several subcategories that were to be considered in making the decision.

Next slide. You notice that mission relevance and consistency is not on here, that's because we didn't give it any points. It was the beginning of the process and if it wasn't consistent with your

mission, then you just didn't do it. So we weighted everything, ten points for importance, ten points for preventability, feasability and then five points if we felt there was metric to evaluate it.

Next slide. With 12 participants and a top score of 35, you could get a maximum of 420. The scores for the different things range from 90 to 308.

Next slide. We rated these -- these are listed in alphabetical order. I won't read them obviously. They are in the briefing package that you have.

Next slide. The top ten were number one, physical training related injuries followed by privately owned vehicles, athletics and sports, excessive heat, motor vehicles, falls, jumps and on down the line.

Then we went back and because the safety centers are doing a lot with POVs and also the national highway traffic safety administration and the academic institutions and the CDC, we didn't feel that it behooved us to look and pursue that intensely. Excessive heat, there's a whole institute that deals with environmental injuries where Paul Amoroso comes from and where I once did research, the Army Research Institute and Environmental Medicine. So we weren't going to do that. And these by the way are CHPPM priorities for Army Injury

Prevention. So these are our internal priorities.

Several groups have used a similar process and it is amazing how some of the things they come up with are.

Next slide. That gets us now to the military training task force you saw -- data like you saw here, and also the results of that prioritization process. They did their own -- had their own work group, the Joint Services Physical Training Injury Prevention Work Group applied a similar process. They have written a white paper that is being sent forward to the Defense Safety Oversite Council as one of the recommended strategies for approaching injuries. It hasn't been accepted yet. I would expect that some version of it probably will be employed and in fact Health Affairs uses a very similar process, which I think has been very productive. The chairman and the task force envision working down the pyramid, which makes good sense, looking at severe -- looking at fatal injuries, motor vehicle crashes, the primary focus; severe and not fatal injuries, falls; and duty limiting injuries, physical training and sports. And looking for off the shelf proven solutions through a systematic review process.

Next slide. Motor vehicle crashes can occur anywhere, not just on our highways as we see here. This

is a crash of a Humvee in the theater. Next slide. And not just in hot weather, but these things come in cold weather as well, as we see here.

Next slide. Some of the recommended, these are empirical base solutions and I say that because they aren't strictly done off of intervention trials or program evaluations, but really sort of a safety approach cluster analysis as groups of crashes that have things in common, and route cause analysis. Some of the solutions that are being recommended are seat belts, digital solutions, better GIS systems, roll-over protection, communications systems within the vehicle and better egress. The doors from the up armored vehicles weigh 250 pounds. So if you're upended and have to push up, it's not easy to get out of the vehicle.

Roll-over prevention is of particular importance because there's been a fair number or roll-overs. They support simulators and convoy and live fire training, driver training assessment for not just Humvee's but all vehicles, so that we know that the individuals driving them really are current on their training, roll-over specific training. Black boxes to track mileage and circumstances of the vehicle when crashes occur are being explored. Standardization of training across all the services. Joint Tactical Vehicle

Working Group feels that they need to better share practices across the services and to leverage each other's expertise.

Next slide. Falls, as I alluded to before, you can fall off of wheeled vehicles but you can fall off of other types of vehicles, and it's not hard to imagine, you know, working on helicopters and other pieces of equipment in the inventory, how easy it is and they aren't engineered with this kind of activity in mind, necessarily, but they get -- this sort of thing, inspections get done routinely.

Next slide. And there are abundant opportunities to suffer falls from a height while working on military equipment like this tower here.

Next slide. And then mundane things like climbing stairs, here without banisters. So you know, falls may seem complicated but there are things -- 40 percent of falls are from heights. Another 40 percent are from ladders and stairs, from data that was collected in the 90s and I suspect it's fairly similar.

Next slide. Anyway, this -- falls represent a very new priority. The Air Force really took the lead on this. They established it as a priority in 2002 and that identified a bunch of -- a number of potentially modifiable causes. Clearing of ice in parking lots and

on walkways, wet surfaces and floors. I mean, a lot of common sensical things. Oil spills and waxed floors and then working on height -- at heights without proper equipment.

The Army, we knew from work that COL Amoroso had done on falls at about 40 percent of hospitalizations were falls from an elevation. We looked at safety data at the CHPPM we found that the leading cause were human movement 35 percent, physical training 12 percent, sports 12 percent. And if we looked at movement, the leading activities were entering and exiting vehicles. And then climbing and mounting equipment and towers and stuff like that. And then going up and down stairs was 22 percent. One can imagine a number of ways we could prevent these. I'm calling this just modifiable hazards since we don't have the data to show what really works.

Next slide. An area where we do know what works though, is where our biggest problem is, it's physical training. Whether it is Marines -- next slide -- Army or other services, or running on your own.

Next slide. What we know is there are a number of intervention trials now that show that reducing running mileage, gradually increasing running and marching and running in ability groups, not only decreases injury rates substantially, but maintains

physical fitness at or about the same level, and we also know from civilian literature that there are thresholds above which injury rates go up, but physical fitness stays the same or actually goes down. So it makes sense to look for those thresholds in Marine recruit training, the Naval Health Research Center showed that they could reduce stress fractures by 50 percent among Marine recruits with only a two percent reduction in physical fitness at the end of training. The Army more recently has studied a standardized program to do the things described up here and showed that the programs reduced overuse injuries 35 percent and increased past rates, the first time pass rates, by five percent on the PT test. So there's good evidence out there that this works. A quad service leader at physical training injury prevention education package is being produced, and funding has been received for that so that should be happening very soon. A prototype has already been developed. Also it was recommended that we need surveillance. If we're going to prevent these kinds of injuries, we need to be able to monitor routinely. The Army does have such a report. It's a monthly report called the TRIR, the Training Related Injury Report. It's possible to do this for all the services.

Next slide. This is data from the Army

medical surveillance activity. It shows the rates of the training related injuries from 1998 to the present. I'm not going to bother to try and explain why these are all going up, but the data is there and we can track these rates.

Next slide. Sports, sports are ubiquitous even in a theater of operations. There are plenty of opportunities for not only football injuries. Basketball is the leading cause, I believe. Football is you know, second or third. And softball oddly enough is right up there, even in civilian communities. Next slide.

A few evidence-based recommendations that can be made on military and civilian research. Ankle braces for those with a prior injury. The Air Force is looking at this right now. Mouth guards, there's a systematic review that has been done by a military work group that shows that you can significantly reduce mouth injuries for high risk activities like technical training, hand to hand combat and so forth, breakaway bases in softball.

Next slide. And for services specific issues, although they may not be huge, it also makes sense in the course of our investigations, if we find things that work and we know and we know work and are cost effective, it shouldn't matter how big the problem

is, we ought to employ them. And braces are something that I think the cost benefit ratio, just on cost of the brace and medical cost can be recommended. And I won't deal further with that.

Next slide. So what can we conclude, injuries are the ongoing single biggest medical problem of the military. If we are going to be successful, we need to attack it at all levels. Key problems we need to focus again across the types of things that we've looked at, and we need to do it systematically.

Next slide. Some things that we really need if we are going to succeed is one, we need to recognize that there is a large category of injuries that the ICD-9 code book does not get at. These are musculoskeletal conditions like stress fractures, Achilles tendonitis that are coded in the 716 to 739 series as opposed to the 800 series where we traditionally look. The problem with that is they don't get cause coded. We need to cause code all injuries treated in the outpatient visits and to document profiles in order to really know what is happening with these. That is not currently being done, but there is an effort being put forward to do that. We need multidisciplinary work groups to meet routinely to review our problems and priorities and we need to develop criteria for identifying recent priorities as well as

prevention. What we saw was a process for prioritizing program and policies for prevention. Research is a little different. That is a topic for another day.

Next slide. My personal conclusions about the DSOC, despite the metrics not going down as fast as some would like, I think this has been a tremendous success. There's been more going on and more attention paid to injuries in the last two years than in the last 20 years. We have got metrics for tracking things. That is the first step is accountability and knowing whether things are going the way we think that they will. There have been some modest successes with motor vehicle and aviation. I think based on established surveillance systems. And it's the place where we have the most experience and infrastructure. And I think the key thing is there's a recognition all of the way to the top of the department that we need to start looking at nonfatal injuries.

Next slide. Some of our slowest progress has been in military training and operational injuries. It's the most difficult problem. It's the most variable and there's the least data. But this is the place where we have the biggest potential for reductions. We've had some successes as I've described earlier.

I think important initiatives, Health Affairs established a Military Injury Prevention Priorities Work

Group. I think that that work group is making good progress with the systematic approach that is more rigorous than those that have been done previously should help set the media priorities for programs and policies, and also provide the foundation for targeting research, because research right now isn't necessarily targeted on our biggest problem. And finally, we're working on metrics for tracking rates to the installation level. We really need to draw that down to the unit level. It is doable, but the problem with tracking to the unit level is our unit identification codes don't necessarily get us where we want to be right now. But I think it is certainly a fixable problem. Anyway, I'm going to close there. I have another slide but it's redundant with some of the other stuff. Again, I'm glad to have had the opportunity to speak with all of you.

DR. POLAND: Thank you, Colonel.

(Applause.)

DR. POLAND: Okay, any questions? Dr. Lemasters.

DR. LEMASTERS: Very interesting. We just published an article on falls during pregnancy. We found out that during pregnancy one of four women fell during their pregnancy. What we found in some of the risk factors associated with this besides the center of

balance being misplaced and throwing people off balance, but simple things like shoes. Women not wearing rubber soled shoes, but you know, they were wearing leather soled shoes. And shoes without ankle supports. I notice all the people running there had the low cut tennis shoes, but not tennis shoes with higher cut. We were essentially showing that the women during the pregnancy fall at the rate of the elderly population. So that's a really high risk time. And just simple changes in the way they were -- what kind of shoes they were wearing, you know, they fell a lot in also wet spots like in bathroom and guards. But you know, I just wonder, do the military folks wear rubber soled shoes or leather soled shoes and then high top tennis shoes instead of the low cut?

DR. JONES: I think it depends, but I think something that you said is interesting. I mean pregnancy is -- we look at only the adverse health consequences leading to hospitalization. Pregnancy is actually the leading cause of hospitalization. So we have a lot of pregnant soldiers, so the sorts of things you're talking about could be germane to injury prevention. And a lot of this I think, you know, what you just said is common sense. I mean a lot of injury prevention is just knowing that you have a problem. So simply having the data for

much of this can lead to solutions, I think at the unit level. I think some of the most important things that you said is when you look at this, you find that the rates of these injuries are quite high in a group you don't think about. I mean, I hadn't thought about pregnant women before. But if they have rates as high as the elderly and the injuries are even nearly as severe, it's a consequential problem. It sounds like there are some common sense solutions.

DR. POLAND: Bruce, as always, a really interesting story that you told with the data. I guess one thought I was thinking toward the end as you were talking about data and summarizing it. The thought I was having is rather than -- it's on the slide in fact, at the last bullet, tracking rates to installation level. Instead of sort of thinking of the geographic unit experience, thinking about organizing the data in a way that those who've got the authority and responsibility to fix it, and in fact, have the bright light shown on them. I found it interesting that the Secretary of Defense put up the challenge of reducing this experience by 50 percent. I don't know if that question was ever answered. But if you start with the premise that much of this story, many of these injuries are preventable, the fact that they are occurring is in fact, no other way to

say it, preventable waste. Didn't need to happen. It has lots of consequences. So I'm wondering if there is a way that you develop a data summarization roll up capability, you can have it in the line chain of command, have it reviewed as on a dash board, at the highest levels of DoD and talk about it, and share success stories, and really get it visible and expect to run the business of the military in a safe a way as possible.

DR. JONES: If we could get the denominator data down to the unit level in a timely way, I think the desire would be there. Installations are the level to which we can do it right now. I agree with that. I think that that's it, and if you'll give me the last slide, create metrics consistent with accountability at the unit command level. I mean, that's really where we need to go. I think that's doable. It's just a matter of solving some technical problems, because if the commanders are accountable, I think they can find their own solutions. I could give you a lot of examples but we don't have time now, but if you'd invite me back I'd love to do it.

DR. POLAND: Dr. Parkinson.

DR. PARKINSON: Mike Parkinson. Bruce, excellent job. I was thinking that when you say the term research, typically we think about either agent host

environment type research or a biomedical model of risk factors, epidemiologic. I think the research that we might need to do is as much environmental and attitudinal around a unique military culture. Somewhere, when the Army decided that everybody was going to wear a beret, like the green berets, there was some cache that everybody has a function, everybody's a solider. I think what we've not done well in the military, my own two cents, is to say, you know, some things we did very well. I think heat stress for the most part, we said it's a command emphasis, it's a command ownership. We have an environmental system that says it's a red flag day, and everything changes. What if we had that for something that looked like a high injury risk environment, and then a trigger. We just began to say what are bulb glow temperature elements that went into that index that we put up on base, what are it's ops tempo, things having trigger a command emphasis in a way that was more cultural than it was traditional medical, you know what I mean? And I just- - maybe I'm not saying this very well. But I don't think we got that old, it's a unique military things, about why is it cool -- you know, if Special Ops had started saying, oh, I would never be on Delta Force without using an ankle brace. It's kind of like how we market it, whether we put it first rather

than where we accept the evidence to just take it off. It's public health generally, but really if you're in the military, you need to do a better job.

DR. JONES: I think some of this is sort of shaping the problem and the solution so that they are acceptable. I mean we are all -- commanders are learning risk management in a way they never had before. And I think as that education seeps through, and we provide them with the information that shows what they do actually causes these things to happen, and that by being observant of the environment that they are operating in and training in, that they can change it. I think you are right. And some of this is changing the culture and changing what's important to them. Because this is as big an enemy as the human enemy when you look at the total casualties. Maybe even bigger. It's not as lethal as a human enemy, but it's certainly causing as much or more morbidity and cost to the service. So I think it's a matter of getting the information out there. And then when I started doing this 20 years ago, we had some studies that showed how to prevent training injuries, and it's only been in the last three or four years that it's been employed. So one of the things that I have learned is that change takes time. Hopefully not that long. I think we've gained some momentum here so

that other things can move forward more quickly. But you make change progressively and cultural and behavioral changes are needed and those are notoriously the hardest things to get at.

DR. POLAND: Okay, I think we better top here. We'll take a ten minute biologic break and reconvene at 4:00.

(Break at 3:49 p.m. Reconvened at 4:05 p.m.)

DR. POLAND: We are going to be hearing a second set of questions for the Board. Col Mike Snedecor is with us today to present a question on Trainee Health Surveillance. The Board has heard some concerns relating to trainee and recruit health and we've been fortunate enough to have had the opportunity to view and tour some of the training facilities and exercises. Injuries sustained by these young people during their training period are of a particular concern. As we go through the next presentations, I will ask that you pull from those experiences and the tours that we have had and consider them in the discussions that we will have this afternoon. So Colonel, thank you. Your slides I believe are at what Tab -- Tab 8.

By the way, in terms of the heat, evidently what's happened is they fired up the boiler this morning, and even though it's turned off the water is still hot in

there, so. Just think of it as a suffer fest.

COL GIBSON: For the Board members, the question from the Air Force on Recruit and Surveillance is in the beginning of Tab 8.

DR. POLAND: If each of the presenters could be as efficient as possible, because as I said, we are an hour behind now and we've got a lot to accomplish. Thank you.

COL SNEDECOR: Good afternoon. I'm COL Mike Snedecor from the Air Force Surgeon General's office. I will be very brief. You have the actual letter, the Board members do, and for the other visitors here, you can read the slide.

Go to the next slide. It's quite simple. Let me just point out that we specifically put trainee in rather than recruit so that we didn't ignore or officer and service academy accession, and their training environments. And also, we do quite a bit of training beyond recruit, where they're doing what we call in the Air Force technical training and more advanced training than the other services. So we don't ignore that training environment there, because there's I think a wealth of opportunity to improve surveillance there and apply interventions. So you can see here, that's the actual question. The next couple of slides, we get to

the specific questions and we can just go through these quickly, because once again you have those and people will be talking to those.

Next slide. And the next one.

And specifically what I, and I would imagine the rest are interested in, is not only an evaluation of what we were doing, but also what we are seeing from the Board, a set of benchmark recommendations that we can sort of use as Emerald City, so we can say, here's what we should be doing. We can do a GAP analysis and say, you know, as we start planning for the future, here's where we need to be, so let's work toward getting there rather than sort of churning what we are currently doing, whether it's working or not.

And also, I'm hoping a least for some recommendations above the service level so that we can start working in concert, working together, have a little direction, focus and maybe funding to help us reach those goals. That's all I have. Any questions.

DR. POLAND: Thank you. Our next speaker then is LTC Bryan Ortman from Lackland Air Force Base.

LTC ORTMAN: It's very much my pleasure to be here and thank you for the invite. It's also very humbling when I see three of my MPH classmates and they are Board members and I am not.

(Laughter.)

You can take this with a grain of salt too probably. But anyway, I do come from Air Education and Training Command.

Next slide please. And at AETC we have 13 and a half bases. We have inherited part of Brooke's Air Force Base, the medical side, so that would make our 14th on the medical part of it. And things are very different at 12 and a half of those bases than they are at one. So the one, the 900 pound guerrilla, if you will, I'm going to talk about today is Lackland. So you can just -- most of you've been to Lackland and you have seen the picture of Wilford Hall Medical Center over on one side, and then you've got the recruit side, the 37 Training Wing on the other side of the street, basically, where our roughly 40,000 year of accessions come through. So there are really two completely different animals. So today we will talk about each of these areas and some of them a little bit superficially.

Next slide please. The first one is just to show you basically what we have in accessions in that it typically runs about 5,000 a month, of any that are on board at any one time, and we will see roughly a thousand a week that --

COL GIBSON: If I could interrupt you for

just a second. Those first two slides are from the academy. They are in your briefing book for background. If you turn just a couple more pages you will find Bryan's slides. Sorry.

LTC ORTMAN: That's okay. As long as we're all square here. So we've got about 5,000 on board for these years, and then it dips down last year to, you know, about 2,500 on board because our accession totals were not quite half, or a little more than half of what they were in years past. Now they are coming back up. so our projections are we're going to be right back in that 40,000 range for the next three years. So that will become a little bit more important as we go to the next slides.

Next slide please. And just to show that our demographics don't change year to year much at all. So you can go through those in your own time. But you know, it stays about 24 percent females, about 30 percent minorities and everything stays about the same.

Next slide please. Now, when these folks get to us in accession in our week zero, and this needs to be moved over one notch, because this is truly right at six and a half weeks of basic training which -- oh by the way, there are studies underway to make it longer, because we just can't fit everything in to get them trained to go

into the deployment cycles. But right now it's six and a half weeks and it has been for quite some time. So all of these tests are done in week zero.

Sickle cell, we have about 1.6 percent of our population that is positive for sickle cell, so that will come forth in a test that we've looked at those folks and studied. We have about three percent who come in pregnant and then go home. We've got about 47 percent that are Hepatitis B antibody positive. So we don't need to vaccinate them for Hepatitis B. And we'll get back to that is as it relates to Hepatitis A in a moment. We'll look at the rest of this as it become a little more relevant.

Next slide. So these are the immunizations that we give and in what time frame we give them. So we're looking at down here they don't quite say. Only 53 percent of that population actually gets a Hepatitis B series. And the Hepatitis A series, we don't know how many come to us Hepatitis A immune already. That would be an interesting study to look at, because it is fairly cheap to test and fairly expensive to vaccinate. So we would like to look at that sometime in the future.

Next slide. So just recently back in April, the training wing said, well let's not allow voluntary separation for our sickle cell trait positive trainees.

So back to his 1.6 percent of the whole population. So they instituted then that no longer could you just raise your hand and say, well I'm sickle cell trait positive. Now I'd like to get out. Because you know, this is a very difficult six and a half weeks. And if you're at the third week of it, you're about as depressed as you've ever been in your life, they're all trying to get out of this training environment. Because it's tough. It's something they've never seen before. And so, now they can't do that. And the proof has been in the pudding that they have not been at any more negative outcome from heat injury or illness because of this. So it's a been a very -- looks like a very positive step. So we recruited good people and were able to keep them even if they are sickle cell trait positive.

Next slide please. This one gets, I think, pretty interesting. The idea was back, you know, back in about 2000 we started strep prophylaxis only in the October to the first of April time frame. And so everybody got basically a big Penicillin shot in the rear. And that would help our febrile illness rates. This is currently then what we are doing. We went to year round prophylaxis in July of '04. They are then administered this big shot in the rear the first week of training, and if they have any history that they're

Penicillin sensitive then we go to one of the alternatives. They self-report that somewhere between three and eight percent of them have had an allergic reaction to Penicillin in the past. And if we do the math, this, on a typical training year of about 40,000 accessions, then this amounts to about eight people that have a serious anaphylactic reaction. No deaths. They've all recovered quickly, but they have had a reaction.

Next slide. This is the really interesting part, where before we started the year round prophylaxis, we had these, you know, valleys and spikes that were all off the map, two range probably, one and a half to two range of the rate per one hundred BMTs per week. This is listed per month, but it's actually per week, if you could break it all out down in here. And so after the Penicillin prophylaxis was instituted year round, it just dropped dramatically and it has stayed dramatically low. So that's without any other vaccinations added or changed. Back in this range, in here, there were some changes that occurred, such as more frequent hand-washing, making sure that they slept head to toe, their blankets were always washed in between groups that came in and some of that was less than optimal in the past. But now that is really optimized back in here. So

all these common prevention measures are in place and unchanged now. And so we're staying at a very low rate for febrile respiratory illness. So food for thought on what's going on there.

Now, this not only greatly reduces the medical care that's provided, but the behavioral attrition that starts resulting when these members are put into medical hold if they're that ill. So because they have to be recycled, and they lose that momentum and steam, that they're waiting to get back to the end of that six weeks and be very proud of themselves, and get in to the regular Air Force, or Guard or Reserve, whichever, that they have had the motivation to do. When they lose that head of steam it is tough on them to be in medical hold. So the attrition rate then goes up.

Next slide. Now I was asked to just mention a little bit about existing resources and this is not a good news story to me. We had more resources applied toward provision measures and surveillance measure in the past than what we have now. And we just don't have the available manpower. But we do have two people full time there and CPT Warback is with me today, she has been at the program for roughly two years. So is really my brain trust to answer some of the tough questions that you might have at the end of the briefing. I will get back

to why I think we need some help in parts of this.

The available databases that we have is one part that is as weak link. The Air Wing data base has all the demographics in it and for what it's designed to do, it's pretty good. The CHCS database coding has gone up dramatically in the last couple years and the database is getting more reliable to look at for all of the illness and injuries that come through. But it is not there yet, and the two are not integrated.

Next slide please. Now, the surveillance that we do, we look at all these types of diseases and injuries. And I would have to say our strengths really lay in this area. Let's just call it communicable diseases, always gastrointestinal ailments. So our strengths really rely -- in those areas, communicable disease surveillance. Heat and injury surveillance is also quite good. Injuries for stress fractures, we're lacking the depth of data that we need in our data bases tied together, so that we can tell you who and why we're having changes, so that we can go to prevention measures that make sense for certain populations. And the same thing holds true with behavioral illnesses.

Next slide please. Now switching gears a little bit on current research projects, the GC/Chlamydia testing for females is actually already started. And

that's moving along quite nicely. No hangups there. So they get urine tested in the first week, all the females do. We think that that prevalence is going to be somewhere around eight percent. And then if they're positive, we go ahead and educate, treat, and ask them to contact their partners, so that they can also seek treatment. That is an area that is right to expand that to male trainees in the future if we're given that task. Comes with a little money trail, but not that much. We'd like to do that.

The stress fracture and prevention rehabilitation program; they are using shoe inserts for in certain cases to prevent lower leg injuries. That's ongoing research. There is more that needs to be done in that area.

Great improvements in the last six months in trying to reduce this time in medical hold. Then therefore lead to lower attrition rates. One of the projects that the training wing was quite interested in was looking at canteens versus camel backs, thinking that possibly that would help prevent illness and injury rates. So that's different -- there are different views of whether or not that is the research that we ought to be conducting, because you know, you've got a person wearing a canteen anyway. And this way they have camel

back instead. So more water, possibly colder water, a little more easy to access. So that will be interesting to see if it truly does resolve in this or not. But that's underway.

The physical training footwear study; basically what this is looking at is the types of tennis shoes that are offered to our recruits, and in place of say one type of tennis shoe fits all, there may be different types of tennis shoes that are needed depending on the nature of your foot. So that one's underway.

And COL Bunning, who is in large part, he is the 59 AMDS or Air Medical Squadron Commander that's put together a lot of these slides. If you're interested in what he is looking at and descriptive epidemiology studies, I've got his card and you can get a hold of him. So there should be something that he is hoping to publish later on on this one. Probably maybe six months from now is my guess.

Next slide please. So where are we at in future surveillance versus where we are at here. Well, if you draw a line right through this, these three above are basically line supplied data programs. And this one is the medical side. And we need to tie these three together so that we can have longitudinal epi studies that we can rely on. So as our coding is now getting

fairly good in CHCS, and this data is wonderful for what it's meant to be, as is this one. We need some help to tie those together and have long term, not home grown data base collection techniques. So that's a challenge that we've got.

Next slide please. So I think I've already said most of that in the prior slides. We're just trying to get into better granularity. Let me give you an example. As I recently looked at why medical attrition in basic training has gone up, it became very obvious that it's related to gender, and the component of the Air Force that they are from, whether that be Guard, Reserve or active duty. So this is just in our new accessions coming in. And we don't have the depth of data that we need to say, is it related to age? We could get there. It is not too hard to ferret that one out. I might have that answer in two or three weeks. But I don't have it today. Is it related to body mass index? It could be because we think we are seeing heavier recruits coming in on average.

Dr. Parkinson, your comment at the break was force equals mass times acceleration, so --

DR. PARKINSON: I just thought that up.

(Laughter.)

LTC ORTMAN: But you would think that that

could lead the more lower extremity injuries. And that's one of the things we think we're seeing, is more lower extremity injuries. Okay. It comes down to, we're asking for your endorsement. And this has been alluded to in a couple other lectures, and by COL Snedecor just before me. So I'll leave it at that. But we do -- we're looking for your endorsement.

Next slide. Now not to leave out the other training sites, because they're important too, but they definitely aren't the big dog on the block. And this type of a longitudinal data base, if you will, could be used at the other sites as well. So if it's Maxwell Air Force Base where all of our officers come through for accessions, or if it is at the follow on training, that everyone goes through after their basic training, then because, you know, our attrition, our medical attrition doesn't just stop at basic training. So we would like to be able to follow that on for say the next four months as they go to Brooke's Air Force Base or Shepard Air Force Base, or wherever it might be for their further training. So these are the available databases at these other sites. And you'll see the same story, CHCS would rely on. Essence, which is just a compilation basically of CHCS data, so we can do communicable disease surveillance. And then certain spools that we run to try

to keep us up to speed on what's going on more quickly. So that's what's out there. The part I didn't put in here is the manpower. Having just come from base level at Ramstein, my little story is, you come to Christmas vacation and your office has been running lean and mean for the last eleven months. And you think, ah, it's time to take a break. And then what happens, Pertussis outbreak. So that's how you spend your Christmas vacation is doing a Pertussis outbreak, because there is not enough staff to start this -- you know, to gin this up. And especially the type of staff that you need. When you've got three public health officers at the most in these places, that are trained in actually doing a sputum female. So it's not just data bases. It's someone on staff as well.

But oh, by the way, I probably had more fun doing a Pertussis outbreak than I would have going to Venice.

(Laughter.)

And I believe that -- if you can believe that yeah. I think that's my last slide. Next slide. I do have some acknowledgements.

Next slide please. And so these are the people that have been responsible for what goes on over on the training wing side for medical surveillance in our

BMT population. And they have put together these slides for me for the most part. Any questions that I hope CPT Warback can answer for me.

DR. KAPLAN: I was interested naturally in the slide you showed about the effect of Benzathine penicillin on respiratory disease in general. You probably are aware or one of these people is, that that exactly parallels what John Brundage describes in the Army -- from Fort Knox about four or five years ago, I think, where they didn't -- they had no explanation for what they found, exactly what you've shown. You might want to look at that.

DR. GRAY: This is Greg Gray. It was by Gunsenhouser, Jeffery Gunsenhouser, and it's Gunsenhouser, Miller and I think maybe Brundage. But it goes to -- it reinforces or concept that these acute respiratory infections in military trainees probably have concomitant viral bacterial components. And another thing that John Brundage, since we've mentioned him, is champion right now is the concept if you think about bacterial secondary infections in preparing for a flu pandemic. And he's suggesting possibly stockpiling antibiotics against bacteria, antivirals with antibacterials as well as vaccines, just in anticipation for this very same thing.

But getting back to your surveillance system, you know, some of the work that you're proposing, the linkages I think have been done by other groups: The Naval Health Research Center, Margo Krause at the Army. A number of these things, you know, they've got existing efforts. And one wonders if they won't be caught under the umbrella of this new surveillance system DoD Health Affairs is putting together. So these linkages are not new.

DR. HAYWOOD. Except for the penicillin pretreatment, those principles seem to be what we have been advocating for the last ten years.

COL GIBSON: I would concur with Dr. Gray with respect to the linkages. Your future surveillance slide, Bob Williams and I drew that out on a napkin ten years ago. So some of these things, perhaps it's finally time for these databases to come together in a way they can really do some profiling of our soldiers. The other point that I have just got to make is with respect to sickle cell trait. The Board has recommended twice to not test for sickle cell trait. The latest time was two years ago. I am a little disheartened to hear that you are using reflective armbands rather than good physical fitness training and good preventions for all of your airmen, but enough said.

DR. CATTANI: Jackie Cattani. I have a similar comment. The Board has been recommending that screening of males for Chlamydia would be implemented. And I was a little disappointed to see future possible screening, both being somewhat vague in terms of a commitment to that.

DR. SNEDECOR: COL Mike Snedecor. I don't remember hearing the Board making an absolutely, yes, please screen males. It's good science. It's backed up by evidence. We'd like that to happen, but I didn't hear that.

COL GIBSON: The recommendation really asked for that to be done, but doesn't -- it isn't a strong recommendation. We'd like to move toward that. We have some plans or at least from what I'm hearing, there's some plans for some good work in there to validate the cost benefit analysis for males. Up to this point -- I understand there is a new study coming out very shortly that will add to the evidence of valid cost benefit of screening males.

DR. SILVA: Just one point. Isn't this giving away genetic data if we have a reflective band on the sleeve and the other recruits know who they are. We are under a lot of pressure now in the civilian community not to divulge anything that's genetically related, done

in genetic screening.

COL SNEDECOR: Mike Snedecor again. They're not the only ones who get the reflective bands. Someone who has had a previous heat injury or is under treatment for say a cold, they are on decongestants also get the band so that the TIs know, this person, regardless of why, is at increased risk. Please keep an eye on them. They're not the ones you want to be dogging when they're kind of floating behind. You want to keep your eye on them and protect him.

DR. POLAND: Okay, one more. Dr. Lednar.

DR. LEDNAR: I guess just looking at the Air Training Command logo, saying developing America's airmen today for tomorrow, and it's really kind of a future vital signs related plot. And the plot has been added to with temperature respiratory rate, blood pressure, the vital signs and with two additional dimensions. One is body mass index, given the impact of overweight and obesity and what that will do to it's diabetes risk factors, musculoskeletal injury risks, add in BMI. And then also add in a two question depression screen. We were reminded in the earlier briefing that mental health issues, behavior health for hospitalization, suicide among the services, especially if the Air Force seems to be a major area for mortality. So I guess just another

thing to be thinking about, screening for improving the readiness in the future, we can't think you know, just the traditional injury and infectious disease risks .

COL SNEDECOR: Bryan, could you detail the time it takes for when an injury or illness happens to when it would show up on your surveillance system or report or whatever you get --

DR. ORTMAN: I think I better refer that one to my brain trust. She says two weeks.

MS. EMBREY: I just wanted to thank you for raising these issues. I think one of the challenges to the Department and the question that has been asked by the Surgeon General, I think we need to balance the need for data for retrospective analysis and research with the delivery of care, and the episodes of care that we are demanding in the system as it relates to screening. One of the issues that I find with the assistance and guidance of congress is that we have now got an annual requirement to screen for health that we self-imposed as part of the recommendation from this Board, to make sure that we were screening for periodic health for readiness purposes. And we used a number of indicators and we are documenting that and we're implementing that. With congress' guidance, we also just recently issued a policy guidance on separation physicals, including those that

apply to reservists on active duty, which means they get that every time they come off active duty even in the global war on terrorism.

On top of that we have a predeployment and a postdeployment assessment. And we also have a post postdeployment reassessment. When we start doing surveillance and health encounters and screening as we are going in and out of training, we are going to spend all of our time in the clinic and not a lot of the time doing what they're trying to do. So I think we need to be balanced in our approach of how we execute what we execute. We are not sophisticated enough in the department at this time. The electrical medical record is an idea this is coming, but it isn't born yet. We have been in labor for 20 years but we are about to have a baby. It's a breech birth.

(Laughter.)

But we are getting very close. As you pointed out, our codes are becoming more accurate. We have more -- the data in the system is more valid. But as you pointed out, we have safety reports that are not connected to injuries and hospitalizations. We have injury reports that are not connected to the safety reports. We do have health and fitness information that comes from the line, but it is not tied to prevention and

protection measures. There is a need for the surveillance system that we are trying to put together at the OSD level to tie all these things together. So your objective is not lost. But it will take a lot of energy and cooperation from all of the services to make this happen, and right now, we have an agreement that it's a good idea, but we can't get past that. So if the Board wants to endorse anything, it would be to move on, get it going and let's do it. Thank you.

DR. POLAND: Okay. Thank you.

(Applause.)

DR. POLAND: Now we have Ronald Ellyson from the Command Surgeon General's Office, U.S. Army Training and Doctrine Command at Fort Monroe, Virginia. He will provide the Army briefing.

MR. ELLYSON: Thank you. I'm Ron Ellyson. I'm a physician assistant. I work for Doctrine Command and also US Army Accessions Command. TRADOC is a four star command. Accessions Command is a three star command. It's at Fort Monroe, Virginia also. And USAC, we serve on the staff of both headquarters. USAC has the recruiting piece, all the initial military training, basic training, specialty training for enlisted, ROTC. And so the next slide please.

These are all of the Army's schools.

Training -- basic training in four places; Fort Sill, Oklahoma; Fort Leonard Wood, Missouri; Fort Knox, Kentucky; Fort Jackson, South Carolina; and Fort Benning, Georgia. That's where we have reception stations and basic training. And some of these schools are interservice. They're run by either the Air Force or the Navy. And those participate. Fort Sam Houston, Army Medic Center School is under a medical command, which is a separate command equivalent to TRADOC, but they -- we partner with them. Our office ensures that the medical content of courses for nonmedical students, like in first-aid and casualty evacuation and field hygiene are kept up to date. Lessons learned from the theater. And then we also do the surveillance and research oversight. So I get to be here.

Next slide. This is what we train our soldiers to do, to dominate the battlefield. I got this picture from my son who's in -- he's an MP. He's with Georgia National Guard over in Iraq.

Next slide please. These are my surveillance points. And I have one slide for each of these six, so what I'm just putting up here was -- back at the reception station we screen for HIV and then also for .... I can't remember the other thing.

Next slide. State of the youth market. We

were interested in who might be potentially interested in joining the Army. And what might interest him or her, in becoming a soldier, at the same time, is he or she fit mentally and physically for the Army, and then also, the persons who have influence, mostly their parents, how they feel about the Army. So this is marketing. We look at what are some of the characteristics of generation Y, the millennium generation. How much of the time do they wear leather shoes? How much time do they spend on their feet? How much green leafy vegetables do they eat? How much milk do they drink? Do they have mental problems and those kind of things. So the National Institutes and Army Research Lab help us with that.

Next slide. This is a report that we provide to the Commanding General of TRADOC each quarter. This is kind of our target, some of the elements of risk. These five here are what my office staff was asked specifically. And this is similar to what Lieutenant Colonel talked about; training-related injuries, like Dr. Jones talked about; immunization compliance. The better and better we get with METROS, the data system that we enter readiness data, individual medical readiness data, the better we'll be able to tell whether we are immunizing soldiers with the shots they're supposed to have.

Environmental injuries. That's cold and heat injuries. And we've added rhabdomyolysis. For a long time rhabdomyolysis wasn't even its own ICD-9 code. We had to use a different code, but now it's in there and we can include that as part of the requirement for the commanders quarterly report for TRADOC. And then sexually transmitted disease. We can pull information for these from centralized data bases and then a couple of previous speakers have alluded to this. We can -- coming up in another slide or two, we can pull epi data for an installation. We can't sort them by who is a trainee and -- or a student and who is not. For example, when I give an installation, for example, Fort Sill, they have field artillery war fighting units, operational units. And then they have a field artillery school. We can only -- we can find out who was injured and who became ill at Fort Sill, but we can't determine who belongs to TRADOC and who belongs to Forces Command.

Next slide. Army Medical Surveillance Agency provides statistics on all our acute respiratory disease and strep illnesses, and similar to what Lieutenant Colonel showed you.

Next slide. This is what the report looks like, and not that you can read it, but there is one of these for each of the five basic training sites, and this

one happens to be Fort Benning and this is -- they're doing pretty well.

Next slide please. Reportable Medical Events, we get a copy of this each day. And preliminary report comes out -- our MES and then eventually they're entered into -- once they're confirmed, they're entered in the Defense Medical Surveillance System. We can go in and pull those out.

Next slide please. And this just shows -- again, you can't read it, but here is, up at the top, Fort Gordon, a couple of cases of Hepatitis C; Fort Knox, cold weather injuries. This was just from last week, so we're getting cold weather injuries at Fort Knox, Kentucky already. And then Hawaii, heat exhaustion. Primarily we're interested in -- So this is the time of year you get both heat and cold injuries. From these we pull out who is training, try to compare them with seriousness of reports that we get though our headquarters. And then also what the safety office gets. And we look at these mostly for heat injuries during the summer.

Next slide please. Training-related injury report. Again Dr. Jones touched on this. Something that AMSA does for us based on 82 ICD-9 codes. This is for basic trainees only, so far. It's hard enough -- because

we have to pull names and social security numbers out of a training data base, send them to AMSA and AMSA matches those 82 codes with those names.

Next slide please. This is what the report looks like. Again, Fort Benning, Fort Jackson, Fort Knox, Sill, Leonard Wood. And then all of them rolled together.

Next slide please. A couple of things that we like to think that we have institutionalized by now, but we haven't, and this is what other individual locations have come up with. I'll show you on the next slide. This is acute respiratory disease report that Fort Knox came up with. And what it shows, again you can't see it, the unit identification and then what type of barracks it is, and what's the capacity of that barracks, how many soldiers are living in that barracks, how many acute respiratory diseases they have. So particularly during the summer, we get more trainees in, our so-called summer surge, that they tend to get closer together than their 72 square feet of space that they're supposed to have. Then so the preventative medicine service stays in contact with the command, and says, don't do this. Figure out something else. This is an instrument that Fort Leonard Wood came up with. It's a Barracks Inspection Report.

Next slide please. This is one of two slides, two last slides, I just listed the health research. The ARMS Study, Assessment of Recruit Motivation and Strength, started by COL Margo Krause and being continued now by COL Christine Scott from WRAIR, this is the research. It consists of the Harvard Step Test and Incremental Dynamic Lift by males. Guys lift 50 pounds over their head and females 40 pounds, and pushups. This is a better projector for conditions, for motivation. And then for asthma, even it's exertion induced asthma, and then for lower extremity conditions, than sending to process, for example, or even for overweight. There's -- the Accessions Command allow them to, for the purpose of the study, came in overweight. If they can pass the ARMS test, they can come in. I just wanted to show you the step test. This is kind of an 18 inch height. So it's two steps per second for five minutes. (Demonstrating) For five minutes. So you have to be motivated. The Commanding General at Accessions Command was so excited the last time he took a report from COL Krause, that he wanted to adopt it for all of the MEPS. USAC is the executive agent for MEPS. But they wanted to complete the study.

Adenovirus vaccine, we've heard about. Hand-sanitizing, the degree on which emphasis on

hand-sanitizing with hand-sanitizing gel or hand-sanitizing foam actually reduces communicable -- we borrowed from the Navy who have done research in that and the Marines.

Wearing athletic shoes more of the time than combat boots, again an idea we borrowed from another service, the Marine Corps. Some of these lower extremity stress fractures related to foot care, trying to customize too soon to footwear that they haven't been accustomed to, so they spend more time -- wear athletic shoes more of the time and combat boots less of the time, for the first few weeks of training. So it's something they're looking at doing at Fort Leonard Wood. Here they put in a nutritionist, an active duty dietitian at Fort Jackson to study whether providing a more focused diet for things that our soldiers, particularly women are lacking in diets. Higher in calcium, and so on. At Fort Jackson that's coming up. And the standardized physical training program. And again, Dr. Jones touched on this. I was so proud of the Army when they came up with this. This is scripted each day, Army Physical Fitness School came up with this. This is the requirement, here is what you do for warm up and for conditioning and for fitness and for strengthening. And here is what you do on days two, and here's what you do

on day three. And I thought commanders and drill sergeants were going to protest it, this is something that was being taken away from them, only they didn't, because there was really no -- really no physical training manual, they weren't following it. So this time we -- higher quarters has imposed this on them, and I think the reason why we are not seeing a trend of injuries go down, is because at the same time this has been implemented, we have also increased rigor, and realism to the soldier. When they first get to basic training, we say, here, carry a weapon with you now, and wear a kelvar helmet and wear a flack vest and wear a patch. This is what you are going to have to get used to doing. That might have been too much too soon. So it kind of -- it may have kind of cancelled out the effects of our standardized physical training program.

The next slide please. 360 feedback is kind of an exit interview, both for soldiers who are separated for some reason and who can't be in the Army and also for graduates from initial military training, to find out what they think about their training.

Attrition review, the Office of the Surgeon General had deployed the team of an orthopedic consultant and mental health consultants to find out why we are losing so many. So we got some good feedback from that,

and interventions. Self-care initiative, this was touched on earlier, I think, as far as having ready access to a screening facility so that being concern about going to a centralize clinic and spending a lot of time waiting has been worth it's worth.

Women's health initiative is just a nice way of saying that we in the Army, unlike the other services, have a way of fitting the well-woman exam in to either reception or their prebasic training, so that would include probably Chlamydia screening.

Then finally we've been involved with the treatment by the manufacturer of Army combat uniform with permethrin, not rely on the soldier or the leadership to retreat their uniforms with permethrin.

Next slide. Often we start or begin projects we think it's going to be easy. This cartoon is from Stars and Strips, from the World War I era. And then, next slide, we end up -- probably not even at the finish, somewhere halfway along, the end looking like this. That's all I've got. Thank you for your kind attention.

DR. POLAND: Any comments.

DR. LEDNAR: I'm just wondering as DoD is bringing its surveillance together, is there any thought about for the basic training environment, across the services coming up with a standard short set of metrics

looking at them all side by side. I realize the training durations are different and some activities vary, but as a basic entry into the military experience, is there any value of laying them all out to review.

DR. EMBREY: I think that is what the question is.

PROF. BAKER: Sue Baker. You mentioned that physical therapist reporting injury data. Wouldn't it be possible for them while they are getting the injury data, to get one or two words that would tell how the injury occurred, rather than simply what the injury is. I think cause of injury is essential for prevention of injury, which is the biggest health problem.

MR. ELLYSON: That's a good comment and the reason I put physical therapists up there, they -- through patients, they see the ones who are bad enough to go to physical therapy. And they're more consistent in their diagnosis, the diagnosis codes that they use than are primary care providers like me. But you're saying that that would simplify the problem, in other words, the statement of the problem as far as what's wrong with them.

PROF. BAKER: Not just what's wrong, which is the type of injury, what was the cause or the circumstances of injury. Not only for those more

seriously injured, but for the minor ones too.

DR. POLAND: Okay, thank you, Mr. Ellyson.

DR. JONES: I wondered if I could ask you a question. We were enthusiastic about the standardized PT program and still are, and of course we work very closely with you and the Army Physical Fitness School. You mentioned a couple of things that you felt had changed the effectiveness of that program, all having to do with increased operational tempo and desire to train soldiers rapidly and get them into their body armor and stuff. And I don't think that there has been any systematic desire to change that program. On the other hand, in addition to the things that you listed are related to getting recruits and trainees in the Army's vernacular, ready quicker. There are other things like a policy to allow the drill sergeants to conduct remedial PT at their own discretion, and I think -- of course remedial PT for those of you who don't know, is where you take people that are less fit, and you give them remedial training so that they do actually more training than the other trainees, in hopes of getting them in better shape, and of course what you are doing is overtraining. I think the Naval Health Research Center has shown that the individuals who come in to the Marine Corps who are the least fit and least physically active prior to that are

the ones who benefit the most from the programs like you described, where you reduce running mileage and progress running.

Do you think that something like that is happening, because those are in fact the individuals who make the biggest difference in the injury rates; that there are initiatives like that that have really changed the basic program as it was envisioned by GEN Cavin when he implemented it.

MR. ELLYSON: You're asking whether the so-called remedial PT is still there and it is. unfortunately. We put it in policy that you're not supposed to give them additional PT, you're supposed to stay with this standardized PT only. But we ride and visit and find and ask soldiers, and they rat out their leadership. But it's kind of a culture shift that's going to be resolved gradually, I think.

You said that the persons who are less physically fit when they come in are --

DR. JONES: The least physically fit and least physically active on entry to the service, are the ones with the greatest reductions in the injury rates or when we implement a program like the standardized PT. And so one thing like freedom to use remedial PT at their discretion really affects the target group the most. So

it is not surprising. I think that there are a lot of things though, that you've mentioned and what it shows is that progress takes place in evolutions. Because the first year of the surveillance showed that it worked. And what we've seen is as these slight changes in policy have been implemented, the rates are climbing up again. And it's a disappointment. On the other hand, I think we had an early success that shows us that the principles work but we have to keep them in place.

DR. POLAND: Okay. Thank you. We need to move on to CPT Ed Kilbane and the Navy briefing.

CAPT KILBANE: Thank you. This is a briefing from CAPT Jesse Monestersky from Great Lakes. I want to thank him for providing the slides. He's our current PrevMedOfcr at Great Lakes. I'm going to try to cut out quite a few of the slides in terms of time and still get the message across. If you have the next slide, after thanking CPT Monestersky. I asked him what this was and I guess it depicts a page that they originally tried to get into the U.S. Constitution and the writing is faded, but it was the first attempt trying to put in, this page intentionally left blank.

(Laughter)

This is actually the most important slide of my presentation because this is the one where I get to

put it in perspective. The U.S. Navy used to have multiple training sites for enlisted. Now that's all been consolidated at one place, Great Lakes Naval Station, just north of Chicago. We have other training sites that are not for recruits. Most of our major bases have some kind of training going on at them in a formal manner, at a school. For the officers our biggest accession places are at the Naval Academy. Also Newport and at Pensacola. But I am just going to focus on our big one here at Great Lakes to talk about what kind of surveillance we are doing there. I just want to talk about -- the rest of the training, beyond accession is just part of our routine surveillance and however well or poorly you think that works, that is what we do.

The program at Great Lakes was developed locally. It wasn't -- we didn't mandate it from the headquarters level. But the idea was, it was designed to give actionable information about things that could be done at that level. Now the report is shared with our surveillance hub, but it's not something that we routinely monitor at headquarter's level. We let the epidemiologist and the prep med people take care of that. So it's developed locally so that they could add and take away things that they deemed important. That approach is very good for indicating when a peek occurs. When

something is out of the ordinary that they have to investigate or they have to intervene on. It doesn't do much for the basic baseline rates, which are a harder nut to crack anyway. That is what the research is aimed at doing.

So things that have been added recently to this report are things like MRSA and one thing that is of local interest up there the operations run so you will see that in the backup slides.

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Go to the next slide please. What you'll see in the slides in your book basically are the graphic data, but that's just the data. What actually comes out of that is -- I have an example of it, is a 13 page report that's based on the data, and everything gets an analysis, some sort of professional conclusion is made on each category, an intervention is recommended and followed up. So it a complete cycle.

Okay. Next slide. I won't go into any more of this, but typically I had -- at Great Lakes they have about 6,000 new recruits. They have about 1,000 in the Corpsman School, that's the NHCS and there are about 4,000 other students there who are beyond the recruit training. So they have nice denominator data, and then you can see all of the things they follow from that list.

And then if you could go to slide 13, and

again, this is just the graphic data, just keep on going. I don't think it's slide 13. It's the second to last slide.

Beyond the graphic data, there's also some narrative data that is put in about hospitalizations, ambulance runs, and specific notable events. Also in the Great Lakes report they have a section on national trends for instance in flu season they'll have the CDC reports. And also reports from the local county health departments, if anything is going on out in the community. So just a quick run down of what is being done at our major recruit command. Any questions?

DR. POLAND: Dr. Lednar.

DR. LEDNAR: It's I think probably very helpful that the experience is graphically portrayed. I have kind of two questions or maybe suggestions. One is, as you have a number of these points, is providing some sort of help to the person looking at it, whether or not these points are; two things; one changing, an important way to recognize, and then the second is some sense of putting the local experience graphically presented into some context, because it may be that another potential basic training site capturing some of their data is running at a level that's 30 percent lower than yours. So while it looks like it's either, in sort of

homeostasis, or even improving a little bit, it may be that its whole level is higher than perhaps is possible. But you wouldn't know that unless you gave some sort of a graphical signal, even just an arrow, and maybe it's best in training class level.

CPT KILBANE: Again, as I mentioned before, this doesn't really address those baseline questions; Is their baseline a good baseline? It only really gives you an indication when something gets out of whack based on historical experience there. And also, it just -- as far as trying to interpret this data, remember, these are just the graphs that are used. In the report, each graph usually has -- almost always has some sort of assessment for the user. I mean, we don't turn that in. The professional component is in the analysis and the conclusions and the recommendations, and that's what's added in.

So if we were only giving graphs, we would want to obviously beef that up. As far as adding in other baselines to judge against on the graphs, I think that was their local decision for whatever reason.

DR. POLAND: Thank you.

(Applause.)

DR. POLAND: Dave McMillian briefing for the Marine Corps.

CDR McMILLIAN: The Navy runs the clinics at Marine Corps Recruit Depot, so there will be amazing similarities between the Marine Corps.

Next slide. Just a quick overview of just some of the basic stuff we are going to cover. We'll try to make this quickly.

Next slide. Two training sites. The key difference, Parris Island is the only female recruit training site. You see a few more people, and definitely climatic differences between the two sites.

Next slide. Initial screening. Most of this is just to kind of get a baseline in the medical record type stuff. Not a lot of this is actionable at the local level except when you get down to next from the bottom, the heat injury, MRSA and so forth, the ones that are monitored locally. The Recruit Assessment Program is just par to the overarching program to kind of collect some data from these recruits when they come through.

Next slide. Heat injury at both locations is taken very seriously. They actually do sample urinalysis during one of the phases at the -- phase where they actually go out to the field, live in the field, have pretty much 20 hour workdays and stuff. So this is where their heaviest stress is. And monitor that closely with commands and then basically follow up on anything that

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occurs as a result.

The next thing we look at, next slide, is MRSA. You have been briefed on this before and the Marines are very interested in this. And they are taking action on this. Just as an example, it's been noted that they recommended increasing hand-washing to the Marine Corps, so they dutifully quickly put up dozens of additional soap dispensers. The problem is they had a housekeeping contractor who didn't want to fill them. So they went through about a year of machinations with this contractor to get that taken care of, before we could get soap in their dispensers.

Next slide. Febrile Respiratory Illness, these are things that have been discussed as far as the slides.

Next slide. Where we just look at the rates and this is kind of an internal comparison and actions whenever they see something of note. So this is really not stuff for our level, as CAPT Kilbane said, at headquarters level. It's just more for their local use.

Next slide. Sports medicine and injury prevention is one I've underlined the data collection and tracking, is a part that we are actively working at now. This has been, I think a real success as far as bringing credibility to this kind of stuff and the Marine Corps is

very interested in it. They have in the past made some arbitrary decisions regarding training, and now they have some data that they are coming more and more to rely on. You know, they've kind of come up with these were the drill instructors get together and say, Gee, I just don't think we're being hard enough on them. Now at least they have the data where they can see the consequences of some of that. So we are working on some additional stuff.

Next slide. And on these kind of struck me as administrative movement slide, and I've highlighted here as far as an event that causes a significant amount -- significant percentage of injury. So we're going to be working on this over the next couple of months to try to define the data collection issue here or to find out exactly what this is. Of interest COL Bryan McQuire, who was one of the ones who stood up the Sports Medicine Injury Prevention Program, at the Training And Education Command is now in Iraq, and his replacement was a former commander of the female unit at Parris Island. So she's very interested in this. She's very aware of all these things, and she's ready to work on seeing what we can do.

The next slide is just a little more data. These are just quick snapshots to kind of show you as far as looking at just injury by event and this is a severity

by event. And it's the same kind of criteria.

Next slide is the training and education that's provided during the recruit training. The hygiene and hand-washing is specifically addressed now. And the injury prevention, before entry, we have some of our athletic trainers actually go out to some of the larger recruit areas to kind of instruct recruits on proper training prior to getting to the recruit depot. And they've actually found that to be very well received. You guys know they're fixing to head toward some serious stuff, so that's kind of an extension program that they've been able to accomplish.

And the next slide will be the last.

DR. POLAND: Questions for CRD McMillian. Ms. Embrey.

MS. EMBREY: Quickly and really this would apply to everyone. I've recieved a brief not too long ago that shows that overall, the recruits that we're recruiting differs in body mass index and other kinds of, you know fat and fitness. Fatness and fitness, we're a little softer and less fit than we were several years ago and the question is, do we have any data that shows that and is the fact that we're applying old fitness standards to softer less fit people the problem. And is that why we're instituting these new things? Or is this just

better science for better living?

CRD McMILLIAN: This is an effort to do things smarter for the Marine Corps, plus they've always recognized that a lot of times they would have a person that after five or six years of service and he's starting to become a good asset, that old knee that was a problem ever since he hurt it in recruit training is just not going to get better for him, and they end up losing these guys. So the thought was, well, let's not lose them if we don't have to, as far as to just not smart training. So that's one.

The second thing that is obvious right now for the leadership and the recruiting command is they used to have a fairly long back log before people got to training, so some of these people would have significant improvements in their fitness before they ever showed up. Because the recruiters would get out there and have these guys show up and say, you know, you've got to start working on this. They would actually work them pretty good for several months. Now that pipeline, that back log is getting shorter and shorter. So we are seeing people come in that have had less of an opportunity to get into shape or be forced to get into shape before showing up.

One of the things that we also are looking at

is, they don't do a real baseline physical fitness assessment when they come aboard. They kind of run them just enough to get an idea, this guy is in really good shape and this guy is in really bad shape, but they don't have a solid baseline from which to judge at Delta for their final physical fitness test. So it's always been tough for us to say, you're getting these guys in good shape with x amount of effort, or if we cut back on the amount of effort to reduce the injuries, are we still getting that. Well, they only compare final scores across the board, so you don't really know what you started out with. So you're correct, we don't know that these guys are not in worse shape and we are actually doing more with them. So these are some issues that we are going to try to see if we can convince them to do.

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DR. POLAND: Dr. Shamoo.

DR. SHAMOO: None of this data we've been hearing today includes the National Guard, is that correct? Some of it does? Because I didn't hear any association. Because wouldn't that throw off a little the data.

COL GIBSON: In I believe all of our basic training environments, the Guard train with our active duty folks. Then they go home. But they go through that

initial training right along side ours. They tend to be somewhat older when they come through, but they take the training right along with everybody else.

I want to make sure one comment on this issue of BMI and exercise and injuries, and I realize I got some of the best injury epidemiologists in the world in this room, but my review of the data shows it's not horrendous -- it's not real clear. Different studies show different things with respect to BMI and injury rates. And I think a lot of it has to do with not controlling for the intensity of activity and those sort of things, in those studies. But I have seen strong associations, no associations, and even there's a couple of studies out there that show reverse associations between BMI and injury rates.

DR. POLAND: Thank you, David. We'll round out the service briefings with LCDR Erica Schwartz and the Coast Guard.

LCDR SCHWARTZ: Greetings from the small but hard hitting Coast Guard. This is going to be a very quick presentation.

Next slide please. This is the agenda. Next slide please. We basically have -- the Coast Guard basically has two training centers; one in Cape May, New Jersey; the other is the Coast Guard Academy. Just to

give you an example, in the next slide you'll see, we only have 5,000 recruits for the entire year. I believe the Air Force said they have 5,000 recruits each month. Is that correct?

_____: 40,000 a year.

LCRDR SCHWARTZ: 40,000 a year, so the Coast Guard, is small, people. It's very small. We have an active duty eight week program. We have a reserve basic indoctrination program, which is two weeks. And we have a prior service training program which is about four and a half weeks. And like I said, the goal is about 5,000 recruits. We have a ten percent attrition rate.

Next slide. The Coast Guard Academy, it trains all of our officers, both the cadets, the Officer Candidate School, the Reserve Officer Candidate School, and the Direct Commissioned Officer Training. Our goal is about 950 cadets. We have an attrition rate of about six to eight percent.

Next slide please. I just put this slide up here because I wanted everyone to realize that the Coast Guard is very small, we don't have the clinical support that our sister services have. We have a small clinic at Cape May and we have an even smaller clinic at the Coast Guard Academy. And I put in Swab summer, because that's the summer where the cadets come on board and we're

seeing a lot of injuries and illnesses during that time.

Next slide please. For the record, the Coast Guard Academy does not have any type of injury surveillance. All of the surveillance that we are doing is performed at the training center at Cape May. For injury surveillance, this actually began in 1999 and it expanded slowly throughout the years, depending on the medical officer support, and it's now in a sort of -- I would say fair to midline stage right now in 2005. We have a very, very, very small staff. We have a medical officer who is a sports medicine physician, and she has an athletic trainer who works with her. And we basically -- they utilize a musculoskeletal injury sheet, which is collected by the athletic trainer and it's completed by the corpsman or the medical officer. The information is compiled and it's stored on an Access database. And they present the data, not only to headquarter level, but also to the commanding officer there.

Next slide please. We also are participating in the Febrile Respiratory Illness Surveillance. We've had approximately about 950 specimens submitted. Eighty percent are adenovirus and you'll see in the last slide that I present, Cape May has a very interesting adenovirus that we want to take a look at later on, because we don't know what's happening, but it seems

season to season, it's a very particular virus that's affecting our recruits.

Next slide. STI, we are doing sexually transmitted infection training. We are actually giving them education. All of our females, unfortunately, not our males, are being screened for gonorrhea and Chlamydia. We have a rate of about 3.94 percent for female recruits. And we don't have any type of long term follow-up studies regarding whether STI education is effective currently right now.

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Next slide. These are the two unfortunately only two research initiatives that are going on with the training center at Cape May. And again, it's dependent upon the interest of medical officer on board. Unfortuneately when a PHS officer leaves, then if a new PHS officer comes aboard that's not interested, then the research falls through.

So the two current studies that are being looked at, prevention of lower extremity stress fractures using shock absorbing insoles at training center Cape May. We're not getting much buying from the commanding officer. And febrile respiratory illness from adenovirus also at Cape May.

And the next slide is just the challenges that we're facing. We really are small, small, small,

small force. We have limited medical support. We have limited resources. I am the preventative medicine support and I call CPT Ludwig every now and again. And again, we really don't know what the other services are doing. This is the first time that I'm actually hearing what the Air Force, Navy and Army are doing. So it's unfortunate that we don't have as much communication as the other services. And that's it. Any questions.

(Applause.)

COL GIBSON: One quick comment. You did bring up that you don't really get much feedback from the other services. A few years ago we used to have a recruit symposium and just for the Board's information, the symposium brought together folks who were dealing with recruit training and recruit health issues, and we all met together at one recruit site every year. That is sort of a guide on the volume in the last few years, maybe look toward consideration to stress that in any type of recommendation that you have.

DR. POLAND: Okay, next is LTC David Niebuhr. He is the chief of Accession Medical Standards Analysis and Research Activity at Walter Reed Army Institute of Research Division of Preventative Medicine. He'll brief us on the Armed Forces Recruit Health Research and the Collaborative Opportunities and

Obstacles.

LTC NIEBUHR: I'm going to call the AMSARA for the rest of the briefing, because it's too burdensome to keep repeating. But I am the chief of that. Listed on this first slide are my co-principal investigators for the ARMS study, Assessment Recruit Motivation and Strength study which I'll get to briefly.

Next slide please. This is a good news and bad news story. The bad news is I have 51 slides. The good news is I'm from New York and I can talk quickly, and that's why I think COL Gibson put me on the very last speaker, 15 speakers in one day. I will defer most of this to your reading including all of our information on past studies. I wanted to make a comprehensive briefing for you all. I believe it's been about four years since AMSARA briefed you. Last year with COL Margaret Krause, who has since retired, dealing with sickle cell disease and differences between officers, enlisted accession physicals. And so I guess our cycle is every four years. So I thought it might be good to give you some background.

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Next slide please. So these are the documents and initiatives that were the undergirding of AMSARA.

Next slide please. This is the purpose. It

was established in 1996 at Walter Reed Army Institute of Research to support the DoD Accession Medical Standards Working Group, and what is now called the Army Secretary of Defense Personnel and Readiness MEDPERS Committee, which actually sets the accession standards.

Next slide please. The mission of AMSARA is to develop evidence based medical accessions standards through guiding the improvement of medical and administrative database, epidemiologic analyses, and then integrate policy recommendations considering relevant operational clinical and economic considerations.

Next slide please. These are our objectives. I'll leave that for you to look at later. Next slide please. This is our structure, not to belabor the point but we are situated under a medical research and material command at Walter Reed, within the division of preventative medicine, and most of our manpower are contractors on roll.

Next slide please. This is a snapshot of the (inaudible) that we do for our research. It's truncated at the end of the first tour of duty. Someone said that DoD has an enlisted throw away force. I will show you some evidence to show why that might be true. But ANSARA focuses from left to right from the MEPS station through the end of first tour of duty. Obviously their number

one tour now comes to the -- from the respect of Department of Defense as well as the individual service member, but there for the most part beyond the scope of our research and not at all present today.

Next slide please. So this is a drill down the accession process. You can see that the MEPDPERS committee actually sets the accession standards which are Code 5 and DoD instructions 6130.4 and these accession standards are applied to a primary applicant pool of if you will the primary market of 18 to 24-year-olds, approximately 28 million in the U.S. population. Recruiters have to contract about 11 percent of males and about one percent of females in this cohort every year. So it is quite a burden. There is some qualification/ disqualification going on by recruiters. They obviously have some experience. There is a rejection rate which I left blank, because I don't know what it is. There's no data on it, that -- before you even get to the medical entrance processing stations.

One of the first things I had to learn when I got to AMSARA was that MEPS is not medical entrance processing station, but Military Entrance Processing Station. There's a whole lot that goes on besides the medical exam and that's listed for you there. And just because you're disqualified, doesn't mean you can't come

in. There is a waiver process. We've studied that extensively and that's in your backup slides. And then there's a delayed entry program. And finally, you can come and ship to basic training.

Next slide please. So this slide drills down on the attrition process. Beginning at the MEPS, about a 130,000 active duty and that's correct with most of our research on these slides, are going to be focusing on active duty. I can explain why we focus on that later.

But about 130,000 accessions each year. They reported to one of the uniform services reception stations and we collectively refer to basic and advance individual training as Individual Entry Training, IET. And the attrition is not linear. It's about ten percent during basic training, as you might expect most rigorous. Basic training varies from six weeks in the Air Force to 12 weeks in the Marine Corps. And as I alluded to, obviously it varies in terms of rigor. Advanced Individual Training has a much lower overall attrition rate, about four percent. And again, the length and rigor of that varies also by service and by one of the hundreds of occupations that are out there being trained every day. And then if you're fortunate enough to get through IET and get to your first duty station you then have another 20 percent chance of attrition within the

first four years. And typically service members contract between three and five years of service.

And so when you sum this all up, you have about a 33 percent chance of attrition by the end of your contract that you signed at the MEPS. And on the bottom you can see about a third of all attrition or five percent of all accessions end up in existed prior service discharged for preexisting medical conditions, one of our focus areas of research. And a comparable amount, about four percent have what services call different things, but essentially it is failure to meet performance criteria.

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Next slide please. Just put up all these bullets please. So with over 240,000 medical exams per year 140,000 active duty accessions per year, recruiting costs -- recruiting screening and training costs of approximately $35,000 per enlistee in FY03 dollars, so it's more now. And about 14 percent failing out of IET, and five percent leaving with EPTS conditions, this is right for research and for intervention.

Next slide please. So this is a schematic here that is updated from your slide. My apologies. This is now 1997 to 2002 data, so some of the numbers will vary a little bit and I left the slides with COL Gibson if it's important to you all in your deliberations.

But essentially, about again 240,000

examinations per year at 65 DEFS located throughout the CONUS and PROCONUS about 80 percent of those folks present or appear to be healthy. Now the majority of those are going to be healthy, but some of them either do not know they have medical conditions or are actually actively concealing that. And this makes up about 85 percent of all active duty accessions come from this quote/unquote apparently healthy population.

Alternatively, about 20 percent of these physicals being done at MEPS every day have either a temporary or permanent disqualification and some of them have multiple disqualifications. Now these disqualifications or what MEPS describes as medical failures come in different varieties. Some of them are actually a history of disease or condition that could be either self-reported by the applicant or detected by the physician at the time of examination. About 30,000 of those a year, about a third of those folks enter active duty each year. So either their condition is disproved to be disqualifying through the provision of medical records or consults, or not detected.

Then there's a category of temporary disqualifications. Most commonly this category are overweight or over body fat, and positive urine drug screen most commonly cannabis, about 9,000 a year. And

about 40 percent of those applicants come into the military each year. And then there are dq's for what we call objective tests, things like hearing or fraction blood pressure, about 6,000 a year and about a third of those come in each year.

Next slide please. So let's change the denominator to accession. 140,000 accessions per year. About 85 percent of these folks appear healthy. About 90 percent have a disqualifying condition for a history disease or condition. About four percent have temporary disqualification. About two percent are disqualified based on objective tests. The bottom line I want to take home message for you all is this is, I think a relatively diagram of the system. The existed prior to service discharge rate across these four populations of applicants that have gone through a rather extensive and some would argue, expensive medical examination, is the same. On the order of between five and seven percent. And static. We followed this since 1997 to the present. so there's really been very little intervention, effective intervention in reducing this rate.

Next slide please. So we believe that the current system disqualifies many who can successfully serve in the military, for example, among active duty accessions, about five percent have a waiver for medical

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conditions. We've done waiver studies and the vast majority of these individuals do not receive an EPTS discharge for the waived condition. They may attrite at a little higher rate than the nonwaived, but they don't attrite for the reason they were waived. So in general, the medical process does a pretty good job of screening for that condition. The problem is, doesn't do the sensitivity.

Next the current system fails to identify many with disqualifying conditions. Again, approximately five percent of all accessions end up in existed prior to service discharge. Now when we do case series review of these discharges, very few of these folks were disqualified and waived for that condition at the MEPS. So we're missing at both ends of the curve.

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Next slide please. AMSARA has done a variety of studies again, many of them are highlighted in your backup slides. What I'm going to turn now to is the prospective efficacy trials that are designed to actually challenge accession standards and screening process.

Next slide please. So how do we do our research? Well, we don't have a database so we actually reach out and grab data from multiple sources, which other speakers have alluded to that is necessary in this kind of research.

We get information on military applicants from USMEPCOM, Department of Defense Medical Evaluation Review Board gives similar type data for officers, but because of funding and staff limitations, we don't do a lot of analysis on officers. Service academies again, a potential source of information -- of data rather than a real actual one. We get information from waiver authorities, by diagnosis and hospitalization outpatient data received from other folks. We get existed prior to service discharges from each of the training basis, and through USMEPCOM and disability agencies provides information on their workload. And then finally we get information on gains and losses to the military for all departments, active, reserve and National Guard through Defense Manpower Data Center.

Next slide please. Okay, so this is the meat of what I wanted to talk about. We have two collaborative studies, major collaborative studies in process right now. The first is with USMEPCOM and US Army Accession Command. It is called the Assessment of Recruit Motivation and Strength study. It is funded US Army -- currently funded by US Army Accession Command, USMEPCOM, and the Army National Guard.

The second study, which I'll just mention very quickly in passing is the Small Business Initiative

Research to develop a psychiatric screen for implementation at the MEPS. And this is OSD sponsored research.

Next slide please. Well, I should mention that COL Margaret Krause, retired, conceived and developed this study. As other have mentioned, it is a step test, modified Harvard step test. It is gender specific, 16 inches versus 12 inches for men versus women. It is a timed event five minutes 30 steps per minute. The heart rate is measured one minute post exercise. Difficulties in performing the test were noted by our research assistants. Motivation is definitely, as alluded to, a factor in successfully performing this test. And it's difficult to perform this with lower extremity problems. I will tell you that we have gone over this, that recruiters have built a step, not a chair, but have built a step and have that in their recruiting offices and are actually encouraging future applicants to train on this test to -- if they're serious about getting into the military.

Pushups are in the current test. It's as simple count of the number done in one minute. Mend have to do 15. Women four. And Incremental Dynamic Lift (Military Press), originally utilized by the US Air Force, I understand, for occupational qualification. So

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this press is located in all 65 MEPS. We have provided equipment and again, men have to lift 50 and women 40.

Next slide please. So this is a cohort study. It is conducted at the six MEPS you can see on the slide. We try to get a geographic diversity in our sites, geographically. There are three phases currently to this study. There's IRB approved study by WRAIR. Phases I and II were completed in February. You can see the funders and the cost of the study. Physical performance was tested. Testing was required, but it did not impact on qualification status. So you could pass -- we were in the process of determining a pass and fail, so in phase I and II, we simply require testing and collective data on individuals.

The ARMS -- the purpose of Phase II was to determine ARMS, to predict future attrition morbidity in the general recruit population.

Phase III then was a paradigm shift now. And automatic waiver for overbody fat applicants who passed the ARMS was generated at the located MEPS in these six study sites.

There was an upper limit. Men could have up to 30 percent body fat and women up to 36 percent. Enrollment from February through December with one year follow-up for morbidity and attrition. And as soon as

this study opened up, we had a phenomena called MEP shopping, and we now have overbody fat applicants crossing state lines to get to the nearest MEP study site to test and come into the military. Can't quantify exactly how much that's happening, but we do know it is happening .

Phase IV is where we have submitted a UFR to DA and in this phase we hope to continue the over body fat and add on automatic waivers for selected (to be determined) musculoskeletal conditions who pass the ARMS and I would appreciate any input on this you might have on what those conditions might be. Things that we're thinking about are pain syndromes. So symptomatic fasciitis, retropateller pain syndrome, and the like. As opposed to things that probably would need to get an orthopedic consult.

Next slide please. So here's our sample size calculation. We estimated we'd need about 4,000 Phase III who met weight or body fat and about 11,000 who are over body fat. Early experience with ARMS, we anticipate that a 75 percent pass rate. We expect about 70 percent of those to ship to basic training within a timely period. We assume about 90 percent will remain active duty for at least 60 days, and you can see our -- we estimate about an 87 percent fewer discharge in the

ARMS qualified group compared to those who failed it.

Okay, and then because of larger numbers, about 95 percent probability of detecting a 30 percent difference in attrition between those who are over body fat and those who are within weight and body fat standards.

Next slide. okay, this is very preliminary data as of 12 July. You can see we've got relatively small numbers, especially females. This is cumulative, first injury and you can see we had 54 women who are over body fat, and their attrition, 60 day attrition was 18.5 percent compared to 9.6 percent for those who were within standards. This is not statistically set yet, although there is a suggestion that with more numbers it may well be. And likewise, there was -- the males overbody fat have a little higher attrition, but the effect was not as great as it was seen in females.

Next slide please. This shows the same analysis in terms of relative risk for 60 day attrition. And again, you can see that these findings by gender and all genders, are not statistically set yet, but we have a suspicion that they may well become with larger numbers. But the effect is relatively small. So early results we believe showed no significant increase in risk attrition in those with over body fat and pasted the ARMS test,

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compared to those who were within weight or body fat standards. Now remember, some of those within standards are unfit, so there -- so that group has both fit and unfit. So fit and fat seem to have all the evidence that comparable attrition to not fat and fit and unfit. okay.

Finally, we think about insufficient study population and obviously incomplete longitudinal review of attrition that precludes formation of a definitive conclusions and recommendations.

Next slide. Okay, so what about morbidity. Well, this takes a look at frequency and percentage of first injury in males for Phase III and this is through August of '05 and again this is cumulative, so we've got variable lengths of follow-up in this group. And now we have 165 males that were over body fat. And you can see that when we looked at all injuries by all diagnostic categories or injury types, there was a statistical increased risk of attrition for over body fat compared to males.

Interestingly what we found was the major category that was increased were relatively minor type injuries, such is pain in joint. We were concerned about stress fracture and the fact that being over body fat might be protective for stress fractures and very small numbers there, so we can't have lot of conclusions there.

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Alternatively we were concerned about an increase risk of heat injury and there might be a suggestion that that three percent versus .2 percent, but just too early and too few numbers to do subcategory analysis. But we'll continue to do this as we have more subjects and more follow-up time.

Next slide please. This is the same kind of slide for females now, cumulative again. Again statistically you can see the difference. You can see for any injury and again, pain in the joint seems to have an increased risk in the overbody fat relative to the -- within weight and by the standard. And there's nothing really going on there in terms of heat injuries for women.

Next slide please. okay, here's our relative risk calculations and now you can see they're all significant between 2.1 and 2.3 and this we've -- what we've done here is we've excluded anybody that didn't make it to the 60 days at follow-up. So we're trying to -- this is one attempt to account for variable ways of follow-up. I'll show you another in a minute. Here as opposed to attrition we are already seeing an increased risk for injury. But again, these seem to be mostly minor.

Next slide please. This slide is different

from what's in your handout also. Actually the female more so than the males. But you can see that the pink is the over body fat group. These folks, we had about 265, I believe, individuals who were over body fat, starting out at time zero there, and in this case, we are matched for the number of the mental risk factors for attrition, to include age, race and month and year in which they came into the military. And even when we do that, you can see that we have a little difference. But that the order of difference is about 20 percent by the time to you get to that 60 days of survival.

Next slide. This is the same type of analysis for females. And again, it's statistically significant. The numbers area a lot smaller here. We had about 75 women that started out at time zero that were over body fat. We couldn't match them with as many criteria. We matched only on gender and race here. As we get more cases, we'll improve our sophistication in terms of our analysis. But you can see in this early look, all statistical tests we applied, that these differences are significant.

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Next slide please. So we are observing an increased risk of injury, all cause injury for both males and females who exceed body fat compared to those who are fully qualified.

Leading injuries though seem to be minor, include sprains and pains in the joint. Heat injures and stress fractures in particular seem to be uncommon, but it's early and we have small numbers. So we can't make definitive comparisons at this point in time. And good research always recommends more research. So we recommend more testing and data.

Next slide please. From a DoD perspective, what are some of the potential benefits to adding performance testing. It just seems to make good sense. One of the things we're going to do with trainees is fitness, we might want to test that in the MEPS, but that's just my editorial.

Emphasis on physical fitness prior to entry has to (inaudible) it's biologically plausible. Recruiters can provide information to applicants on how to train, such as you know, having a step test in their office and telling the applicants how they might be able to get in other than fasting and using diuretics, laxatives and other measures that they're currently using.

We certainly do have an epidemic of obesity and overweight in our society. Using enhanced data we think that we could certainly increase the recruiting pool by as much as 33 million. And add maybe 11,000

accessions to basic training.

We do think it's a measure of applicant motivation. And potentially decrease injuries in terms of identifying the more fit as opposed to less fit.

Next slide. So we also have an initiative on psychiatric screening and I'm going to defer that to another time if your interested. I'll stop there and any questions.

(Applause.)

DR. POLAND: Any question from the Board.

DR. PARKINSON: Mike Parkinson. David, excellent. Just to confirm, this is obviously a DoD wide agency and your recommendations go to DoD Health Affairs or do they go to the line or -- okay, they go to Mr. Chu -- Dr. Chu, I'm sorry.

LTC NIEBUHR: That's right.

DR. PARKINSON: Okay, great. That's a wonderful resource.

LTC NIEBUHR: In terms of the ARMS recommendations, this is an Army initiative, Army sponsored research. But in terms of the accession standards, it's DoD.

DR. POLAND: Okay, thank you. I want to thank all of the speakers this afternoon for their superb presentations under less than ideal circumstances. We do

have -- we tried to set aside some time to discuss the presentations. So if there are any overall questions for discussion, we can entertain that now.

DR. SHAMOO: I apologize, when Dr. Silva made his comments about the slide of the silver sleeve I was outside the room, so I didn't know what he was talking about. I went back and looked at the slide. I have really three concerns about that sleeve, reflective sleeve. One is medical privacy. Two genetic privacy. And third, race issues. I would like to ask -- I know in the civilian world answers to all these three questions, but I don't know what it is for the military. Is there a specific instructions about medical privacy and genetic privacy. I know what it is for race because it's the same as the rest of our society probably. So what are the answers for the first two. To me, really, race is not a concern.

COL GIBSON: DoD follows the same principles as everyone else, so they fall under the same regulations, et cetera.

DR. SHAMOO: I mean it's open. It's a big no no then. I don't understand how it slip through -- there is a legal counsel as well as moral counsel in that department or agency or division, whatever it is.

COL UNDERWOOD: I just want to state for the

record that the Army does not screen for sickle cell.

LTC SNEDECOR: This is Mike Snedecor speaking for the Air Force. Just to clarify, the people wearing the armbands are not only people who are Sickle trait positive. The armbands denote people who are at increased risk for heat injury. It could be from a number of factors and there is no way to know what those factors are from your average person there. The TIs just know that if a person has this armband on, they are at increased risk and it's there so that they'll know that if they see them lagging or having trouble or whatever, that they take extra precautions. So I'm not sure how you could assume that just because they have a silver armband on that they're Sickle trait positive.

DR. SHAMOO: If I go by the slide, it says SCT positive trainees requires to wear reflective sleeve. It says nothing about camouflaging it by heat injury. I was outside the room so I don't know what the presenter said, but the slide is very clear. SCT positive trainee required to wear reflective sleeve. So it is SCT. The implication is -- even if it is to be very honest, I would be very careful in term of overall context. Is there any other way to do it with maintaining all of these three issues private, because the sickle cell probably is the -- I don't know what percentage that are for those

who are heat related injuries.

DR. HALPERIN: COL Underwood commented about the Army not doing sickle cell trait testing and the Air Force doing sickle cell trait testing. It seems to be a combination of discussion of medical surveillance as in screening for things as in placement exams, versus surveillance as in public health surveillance, collecting data that you look at for trends, et cetera, et cetera. and then research. And there's no -- there's never an ideal way to do anything, believe me. But you know if we replayed this discussion and had a panel of all of the services talk about continuities and discontinuities in medical screening, we would have faced the fact that the Army does and the Air Force doesn't and et cetera, et cetera. And then, what are the basic surveillance, as in public health surveillance. It would be another discussion where we look at the consistency and inconsistencies. So right now I'm trying to take a table of things that go this way and try to put them this way, and it's kind of a hard thing to do. So it's just an idea for maybe the next round that we do this, that we could do it, by the issue rather than by the service. And maybe even, going to the Dr. Schwartz comment, maybe even ask that the services get together and look for consistencies and inconsistencies and then focus asking

for advice on should we be doing sickle cell trait testing. It's just a different way, maybe next time I'll make the alternative comment.

DR. HAYWOOD: A few years ago the Board considered this problem and the sickle cell issue in great detail and brought in experts from outside to review the whole issue. Most of the experts were against specific identification as opposed to imposing strict rules that would apply to all the service people regarding heat protection. There was a compromise however in terms of the final statement and it seemed to me it would be useful to review that.

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LTC SNEDECOR: I originally actually wanted to add in the accession screening the topic of this question and Roger asked me to separate it and maybe submit it later. But I did the same thing. I went through all of our accession sites when I was chair of our training health work group, and I had everyone list what they did for their accession screening, and it was all over the place. And for a myriad of different reasons, with often no policy backing any of it up. So one of my issues for the Air Force was, let's come to some consensus on why and what we're going to do. And I actually wanted the Board to make those recommendations so that we could maybe standardize across all the

services.

DR. POLAND: Okay, wow. It's been a long day. I think we still plan on meeting in the hotel at 6:45.

COL GIBSON: A few administrative comments.

(Administrative comments were made.)

(Off the record at 5:54 p.m.)B